SOME OBSERVATIONS ON THE BLOOD SUGAR IN DEMENTIA PRAECOX.

by

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INTRODUCTION

The investigation of the blood sugar in insanity has recently been the subject of a considerable amount of research.

The following are some extracts from the literature on the subject.

Bowman (1) investigated 70 normals and found their fasting levels between 0.080% to 0.120% and the average of 24 cases of Dementia Praecox 0.097%.

Raphael & Parsons (2) investigating 11 cases of Dementia Praecox concluded that chronic Dementia Praecox gave delayed tolerance with the initial hyperglycaemia and that depressed cases of Manic Depressive Insanity gave initial hyperglycaemia with definite delayed tolerance.

Kooy (3) administering his carbohydrate as 100 gm. bread and 200 c.c. milk, gave as normal figures 0.098, 0.114, 0.116, 0.104 and 0.102% and found in hebephrenic Dementia Praecox a slight increase.

Drury & Farran Ridge (4) employing Calvert's technique, found in Dementia Praecox that acute cases gave very high and rather broad curves: that female acute cases gave higher curves than male:

that chronic cases gave small low curves and that again the male curves were lower than the female. These results were from 18 cases.

Mann (5) employing Calvert's technique and working on Mental Disorders grouped his results as follows :-

(1) Cases showing blood sugar curves approximate to normal type (maximum values below 0.2%).

(2) Cases showing sustained hyperglycaemia with low blood sugar levels.

(3) Cases showing sustained hyperglycaemia with maximum blood sugar levels within the normal range.

(4) Cases showing sustained hyperglycaemia with high blood sugar levels, i.e., maximum values exceeding 0.18%.

In Group (1) there were 12 Dementia Praecox, in Group (3) 5 Dementia Praecox and in Group (4) 6 Dementia Praecox.

Thus out of 23 cases of Dementia Praecox, 11 show abnormality in delayed return to normal of which 6 were abnormally high as well.

FIRST PART.

METHOD

In the tests carried out for this thesis the patients selected were 50 well marked cases of Dementia Praecox, 25 of either sex and classified into Hebephrenia and Katatonia. They were of varying ages and duration of the disorder and this information, plus the mental state whether excited or depressed at the time of examination, is supplied in a following table.

The investigation was the blood sugar curve following the ingestion of 50 gm. of glucose. Also on 11 of the cases the influence of sympathomimetic and parasympathomimetic drugs on their sugar curve and the influence on blood sugar of pituitary, thyroid and adrenal glands was attempted.

The method employed was Calvert's (6) using pipettes to collect the blood samples.

Quantity of blood taken 0.16 c.c.
Added to Distilled Water 7.3 c.c.
Then $\frac{2}{3}$ N.Sulphuric Acid 0.3 c.c.
10% Sodium Tungstate 0.3 c.c.
Filter.
5 c.c. Filtrate in Calvert Boiling Tube and add 2 c.c. Copper Tartrate Solution.
Immerse in boiling water 6 minutes.

2 c.c. Phosphomolybdic Acid are then added.

Allow to stand 3 to 4 minutes.

Add 3.5 c.c. Distilled Water.

Immerse in cold water 2 to 3 hours to ensure a uniform temperature.

Read in a Kober Colorimeter

Standard Discs 7.5 (Calvert) at 13.7 = 0.15 gms. Glucose.

Calculation $\frac{\text{Factor } 13.7 \times 0.15}{\text{Reading}}$ = % Glucose

Result corrected according to Correction Table (6).

The patient was kept in bed on the morning of the test having had no food since 7 p.m. on the previous evening. The first sample was taken about 8 a.m. and then 50 gm. medicinal glucose were taken in about 200 c.c. water. Samples were then taken every 20 minutes for two hours and any urine passed during the test or day afterwards was kept and examined for sugar and acetone, diacetic acid.

As the first cases were investigated during the early part of the year they were placed on each side of the fire and screened round in order to reduce the effect of low temperature. Cases were examined in pairs.

CASES

MALE

No.	Case.	Age.	Duration.	Excited or Stuporose at time of examination.
1	Hebephrenia	27	Under one and a half years.	Excited.
2	do	31	Over five years.	Excited.
3	Katatonia	43	do	Stuporose.
4	do	25	Under one and a half years.	Stuporose.
5	Hebephrenia	35	Two to five years.	Neither.
6	Katatonia	33	Over five years.	Stuporose.
7	do	29	Two to five years.	Stuporose.
8	do	21	do	Stuporose.
9	Hebephrenia	19	Under one and a half years.	Neither.
10	do	23	do	Neither.
11	Katatonia	25	Over five years.	Stuporose.
12	Hebephrenia	18	Under one and a half years.	Neither.
13	do	19	do	Neither.
14	Katatonia	18	do	Stuporose.
15	Hebephrenia	23	Over five years.	Neither
16	Katatonia	32	do	Stuporose.
17	do	40	Under one and a half years.	Stuporose.
18	Hebephrenia	25	Over five years.	Excited.
19	Katatonia	26	do	Stuporose.
20	Hebephrenia	20	Under one and a half years.	Excited.

No.	Case.	Age.	Duration.	Excited or Stuporose at time of examination.
21	Hebephrenia	25	Over five years.	Excited.
22	do	24	Under one and a half years.	Stuporose.
23	do	24	Two to five years.	Neither.
24	do	24	do	Excited.
25	do	23	Under one and a half years.	Neither.
FEMALE				
26	Katatonia	19	Under one and a half years.	Stuporose.
27	do	22	do	Stuporose.
28	do	43	Over five years.	Stuporose.
29	Hebephrenia	34	do	Stuporose.
30	Katatonia	33	Under one and a half years.	Stuporose.
31	Hebephrenia	30	do	Stuporose.
32	do	28	Over five years.	Excited.
33	Katatonia	22	Two to five years.	Stuporose.
34	Hebephrenia	34	Over five years.	Excited.
35	do	15	Under one and a half years.	Neither.
36	Katatonia	24	do	Stuporose.
37	Hebephrenia	21	do	Neither.
38	do	41	Under one and a half years.	Stuporose.
39	do	20	Two to five years.	Stuporose.
40	Katatonia	23	Under one and a half years.	Excited.
41	do	39	Over five years	Stuporose.

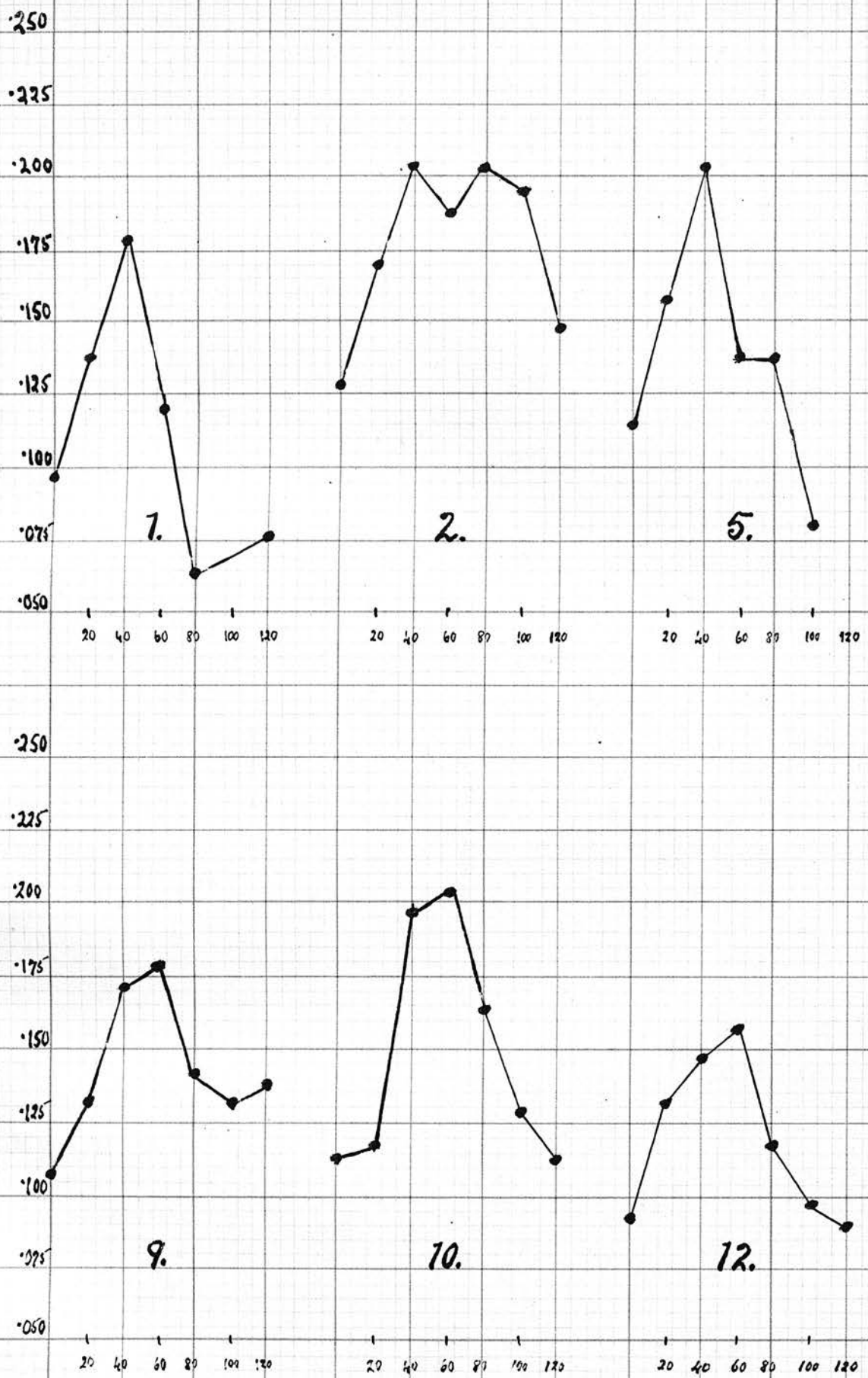
No.	Case.	Age.	Duration.	Excited or Stuporose at time of examination.
42	Hebephrenia	33	Under one and a	Excited.
43	do	26	Two to five years.	Stuporose.
44	do	35	Under one and a half years.	Excited.
45	Katatonia	22	Two to five years.	Stuporose.
46	Hebephrenia	25	Under one and a half years.	Neither.
47	Katatonia	26	Two to five years.	Stuporose.
48	do	34	Over five years.	Stuporose.
49	Hebephrenia	27	Under one and a half years.	Neither.
50	Katatonia	37	Over five years.	Excited.

N.B.
The term stuporose here when applied to Hebephrenia is used for retarded psychomotor activity as in hebephrenic depression; when applied to katatonia it has the usual significance of katatonic stupor.

SUMMARY

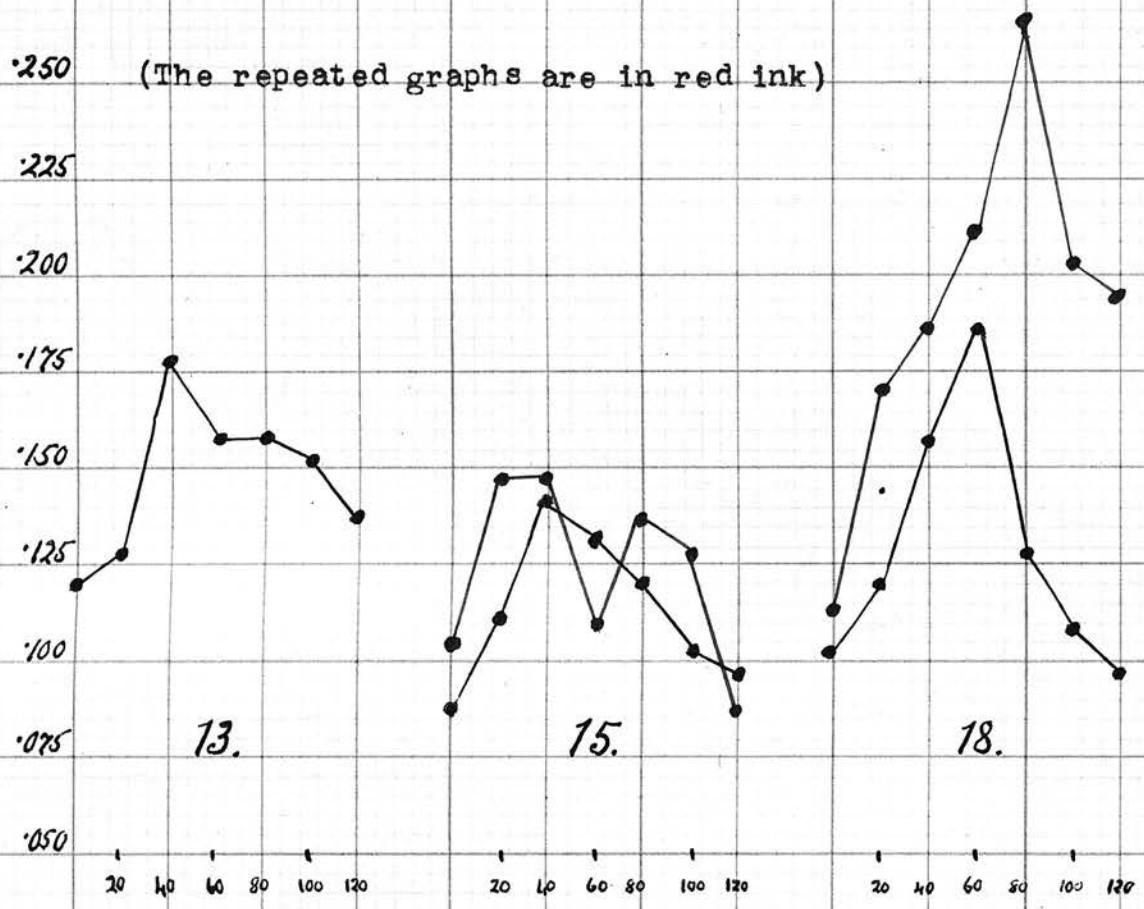
	Katatonia.	Hebephrenia.
25 Male	10	15
25 Female	12	13
	22	28

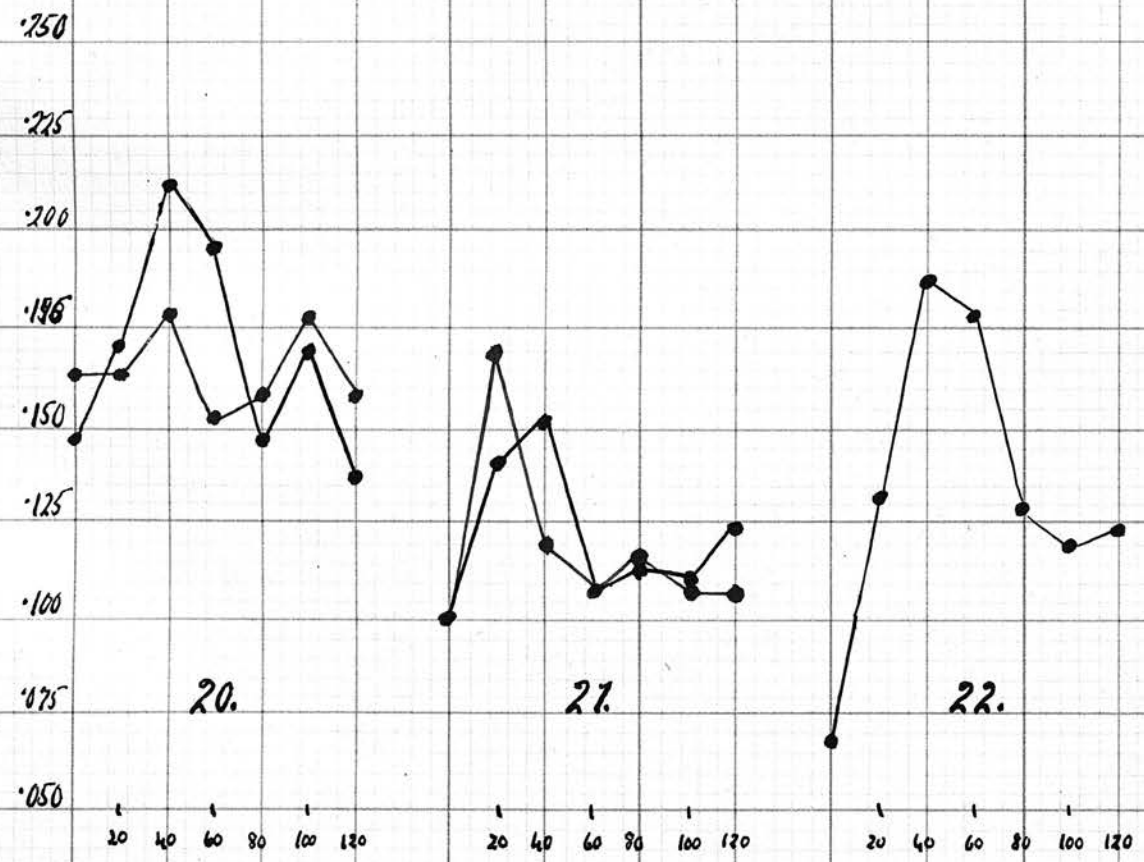
(b)



HEBEPHRENIA (50 gm. Glucose) (Male)

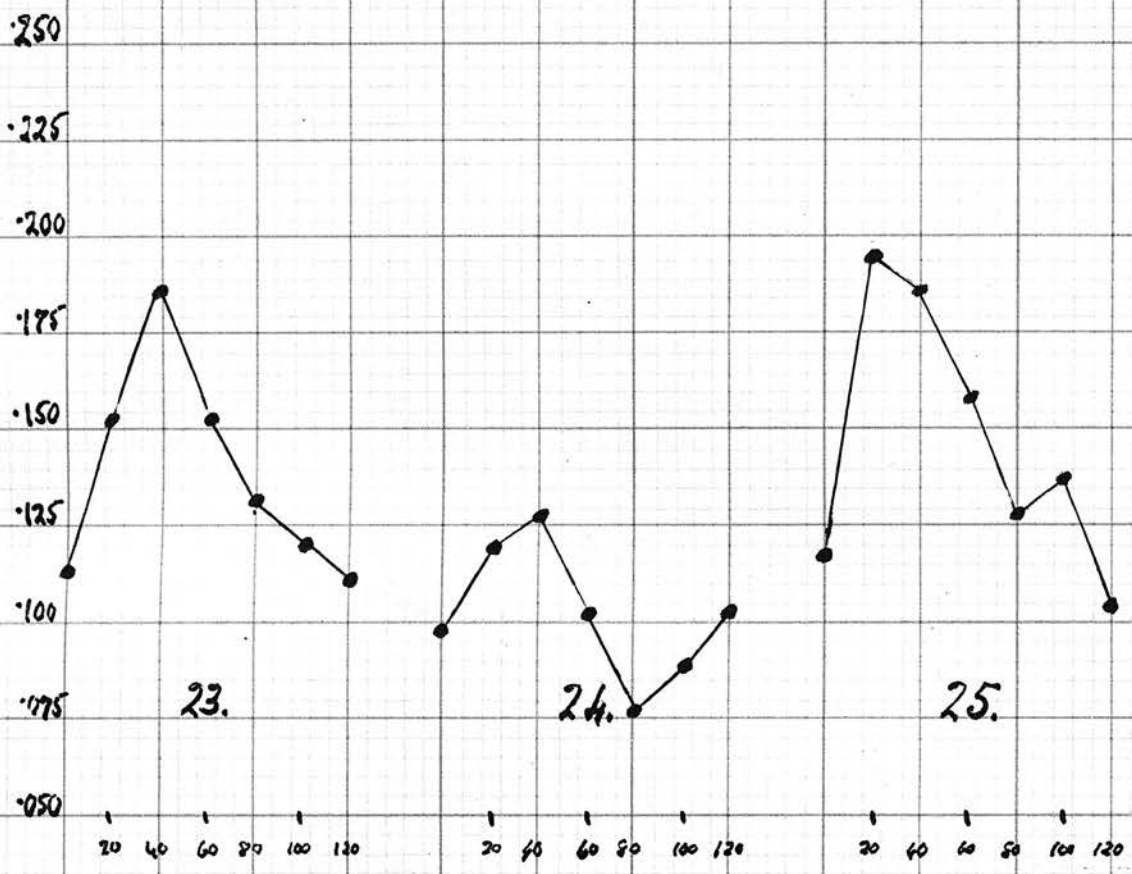
(The repeated graphs are in red ink)





HEBEPHRENIA (50 gm. glucose) (Male)

(d)



HEBEPHRENIA (50 gm. glucose) (Male)

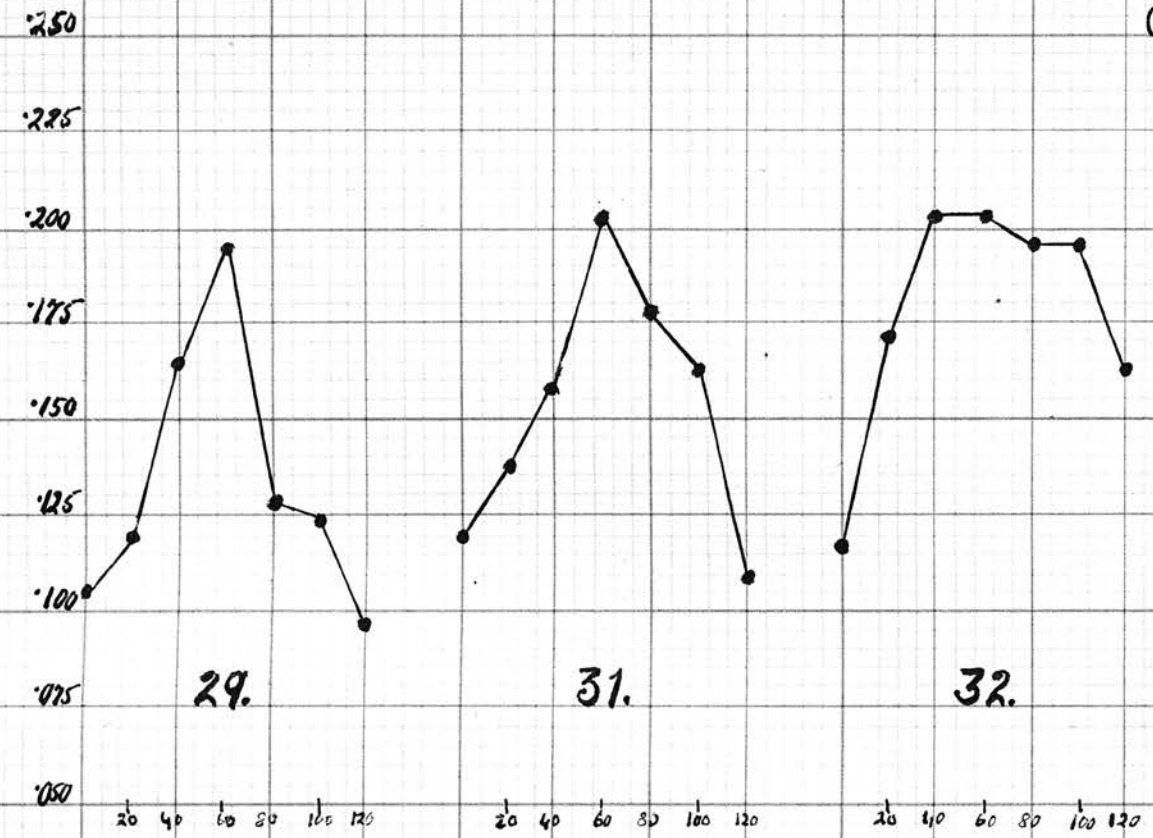
Blood Sugar Values after ingestion of 50 gm. Glucose.

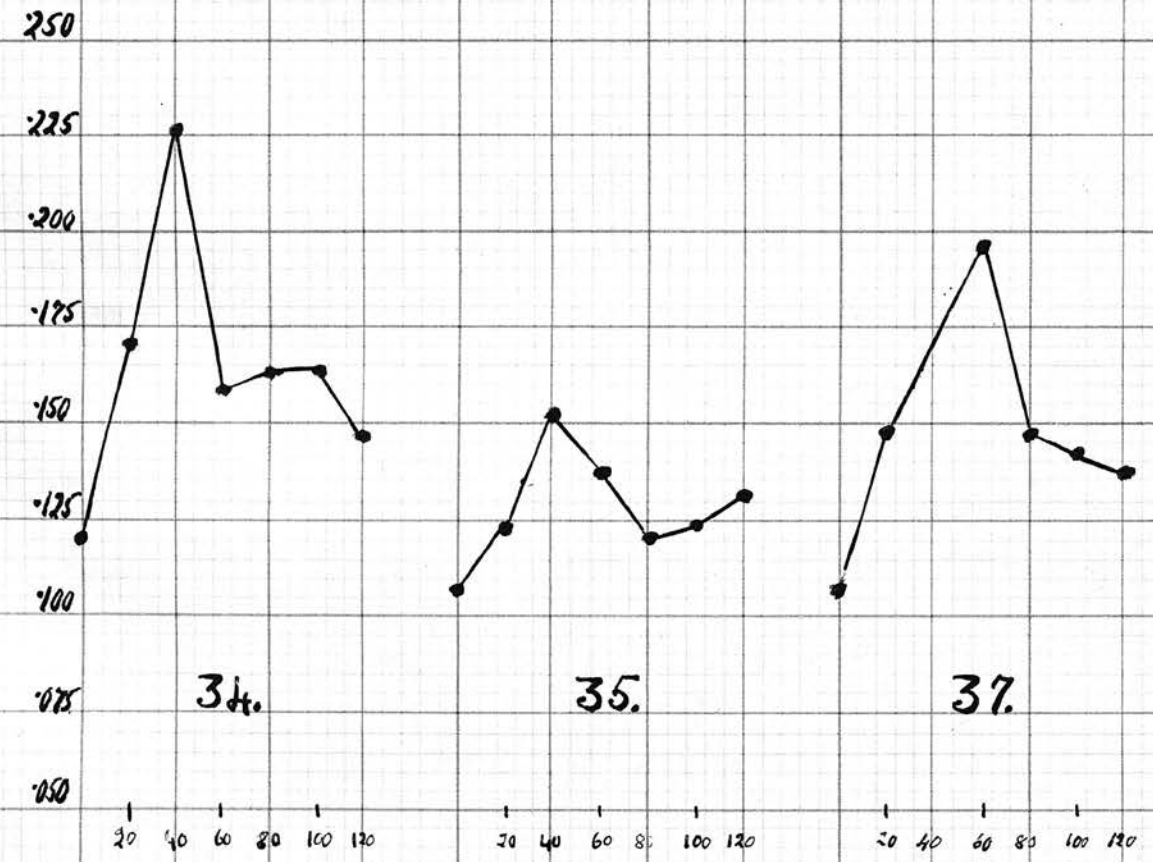
Case	(1) 13.6.25	(2) 8.1.25	(3) 15.1.25	(4) 5.8.25
	0.097	0.128	0.105	0.111
	0.138	0.171	0.138	0.158
	0.179	0.204	0.171	0.171
	0.120	0.187	0.142	0.138
	0.064	0.204	0.114	0.128
	X	0.196	0.120	0.128
	0.076	0.147	0.081	0.117

Case	(5) 25.1.25	(6) 14.1.25	(7) 31.12.24	(8) 5.8.25
	0.114	0.078	0.114	0.109
	0.158	0.128	0.171	0.120
	0.204	0.213	0.171	0.171
	0.138	0.226	0.179	0.158
	0.138	0.226	0.204	0.147
	0.081	0.238	0.196	0.132
	X	0.226	0.187	0.114

Case	(9) 8.8.25	(10) 13.6.25	(11) 13.6.25	(12) 2.8.25
	0.109	0.114	0.102	0.093
	0.132	0.117	0.152	0.132
	0.171	0.196	0.142	0.147
	0.179	0.204	0.132	0.158
	0.142	0.164	0.102	0.117
	0.132	0.128	0.120	0.097
	0.138	0.114	0.105	0.090

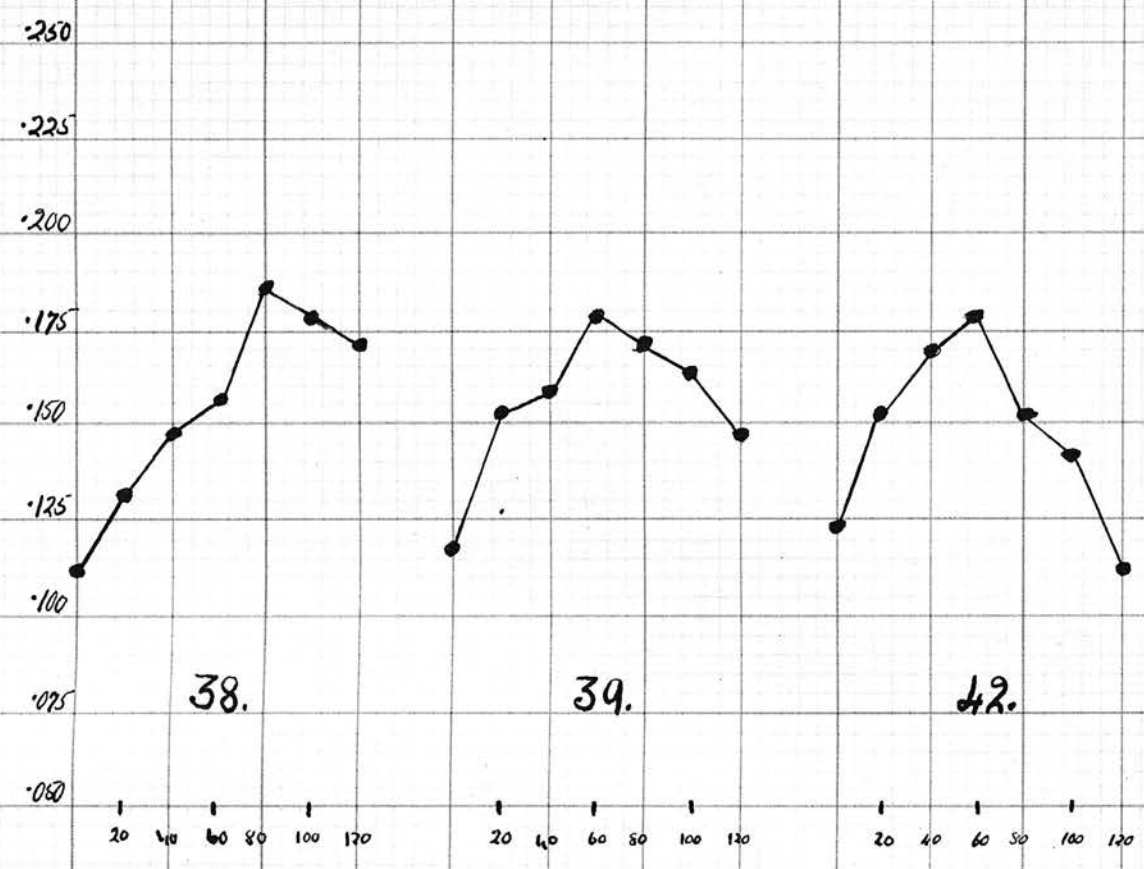
Case	(13) 3.8.25	(14) 19.6.25	(15) 25.2.25	12.8.25
	0.120	0.109	0.087	0.105
	0.128	0.187	0.111	0.147
	0.179	0.204	0.142	0.147
	0.158	0.171	0.132	0.109
	0.158	0.120	0.120	0.138
	0.152	0.124	0.102	0.128
	0.138	0.102	0.097	0.087

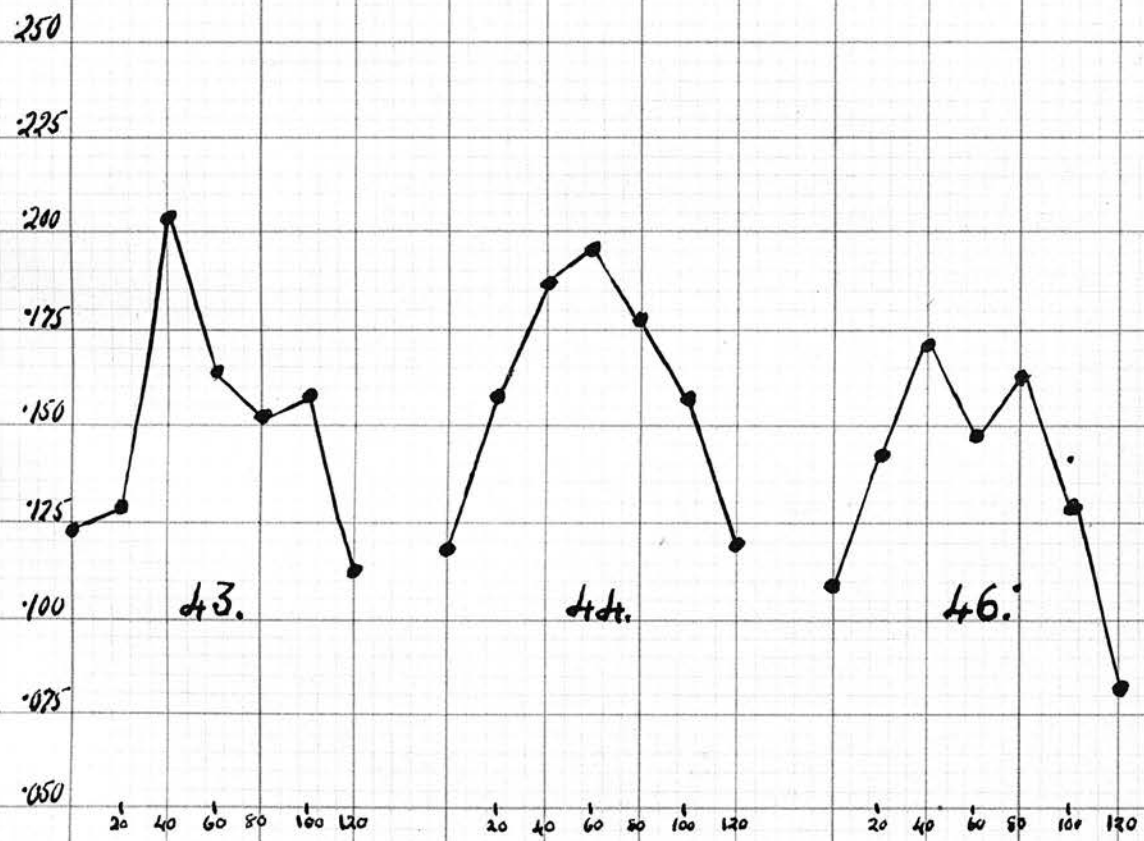




HEBEPHRENIA · (50 gm. Glucose) (Female)

(f)





HEBEPHRENIA (50 gm. Glucose) (Female)

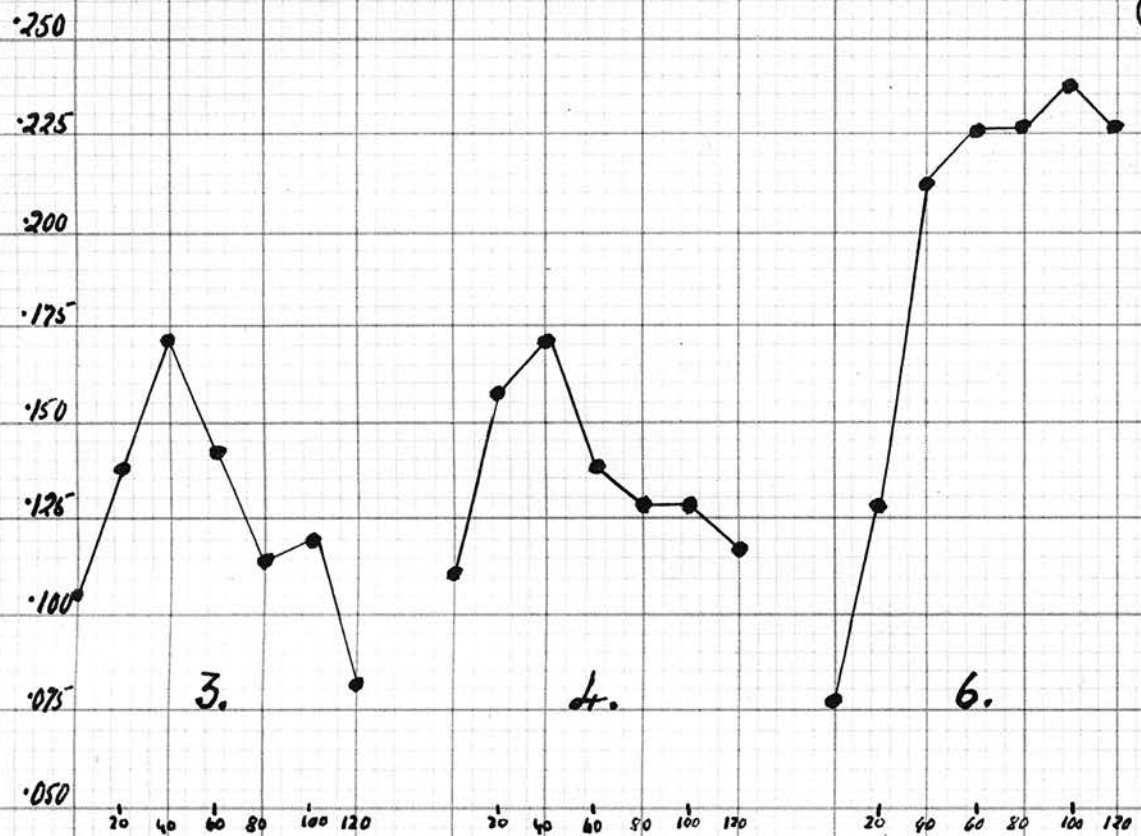
Case (16)		(17)	
25.2.25	12.8.25	22.2.25	7.8.25
0.105	0.099	0.097	0.114
0.138	0.152	0.147	0.158
0.152	0.147	0.152	0.171
0.138	0.089	0.147	0.164
0.114	0.111	0.102	0.171
0.086	0.100	0.099	0.087
0.086	0.093	0.097	0.138

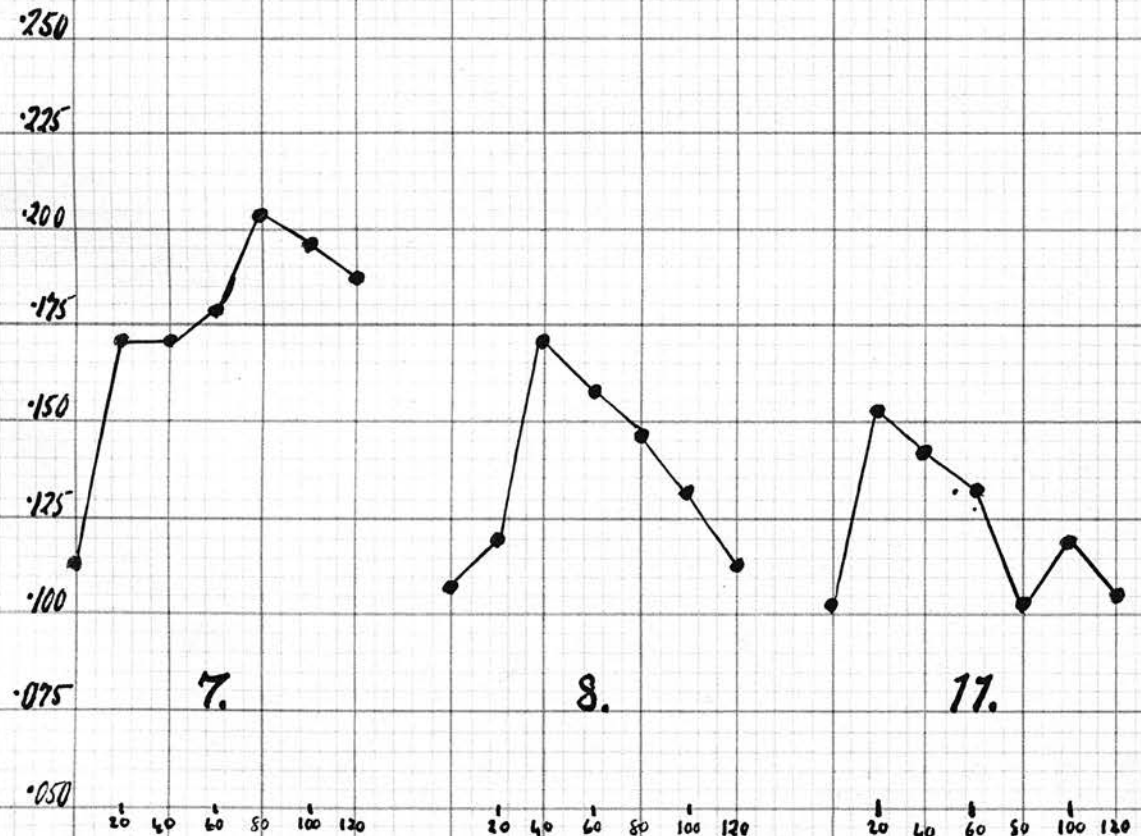
Case (18)		(19)	(20)
22.2.25	7.8.25	2.2.25	13.8.25
0.102	0.114	0.099	0.107
0.120	0.171	0.171	0.171
0.158	0.187	0.179	0.179
0.187	0.213	0.171	0.171
0.128	0.268	0.138	0.109
0.109	0.196	0.120	0.094
0.097	0.196	0.090	0.097

Case (20)		(21)	
6.8.25	15.6.25	5.2.25	13.8.25
0.147	0.064	0.100	0.100
0.171	0.164	0.142	0.171
0.213	0.179	0.152	0.120
0.196	0.152	0.109	0.107
0.147	0.158	0.114	0.124
0.171	0.179	0.111	0.109
0.138	0.158	0.124	0.107

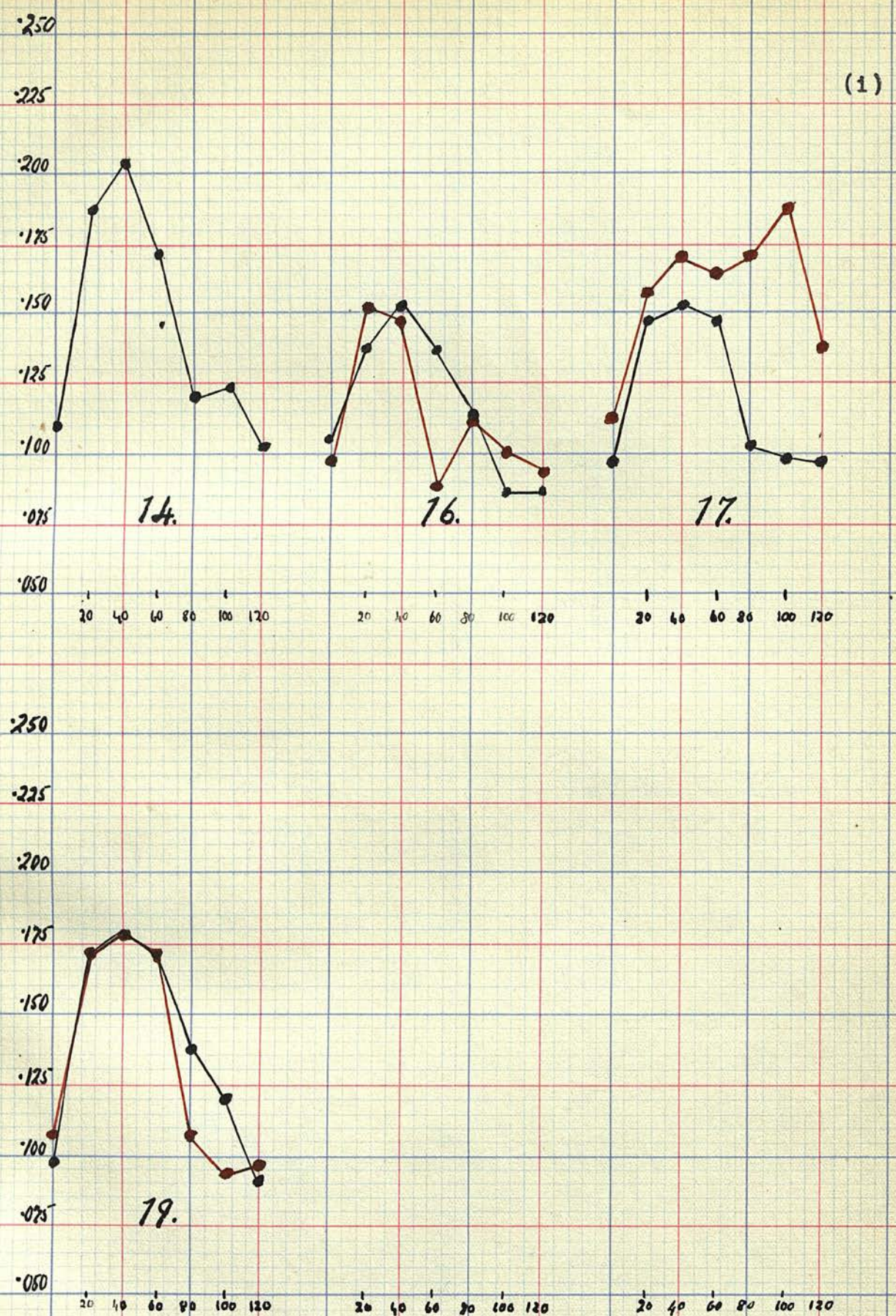
Case (22)	(23)	(24)	(25)
23.6.25	3.8.25	23.6.25	6.8.25
0.069	0.114	0.098	0.117
0.132	0.152	0.120	0.196
0.187	0.187	0.128	0.187
0.179	0.152	0.102	0.158
0.128	0.132	0.077	0.128
0.120	0.120	0.089	0.138
0.124	0.111	0.102	0.105

(h)





KATATONIA (50 gm. Glucose) (Male)



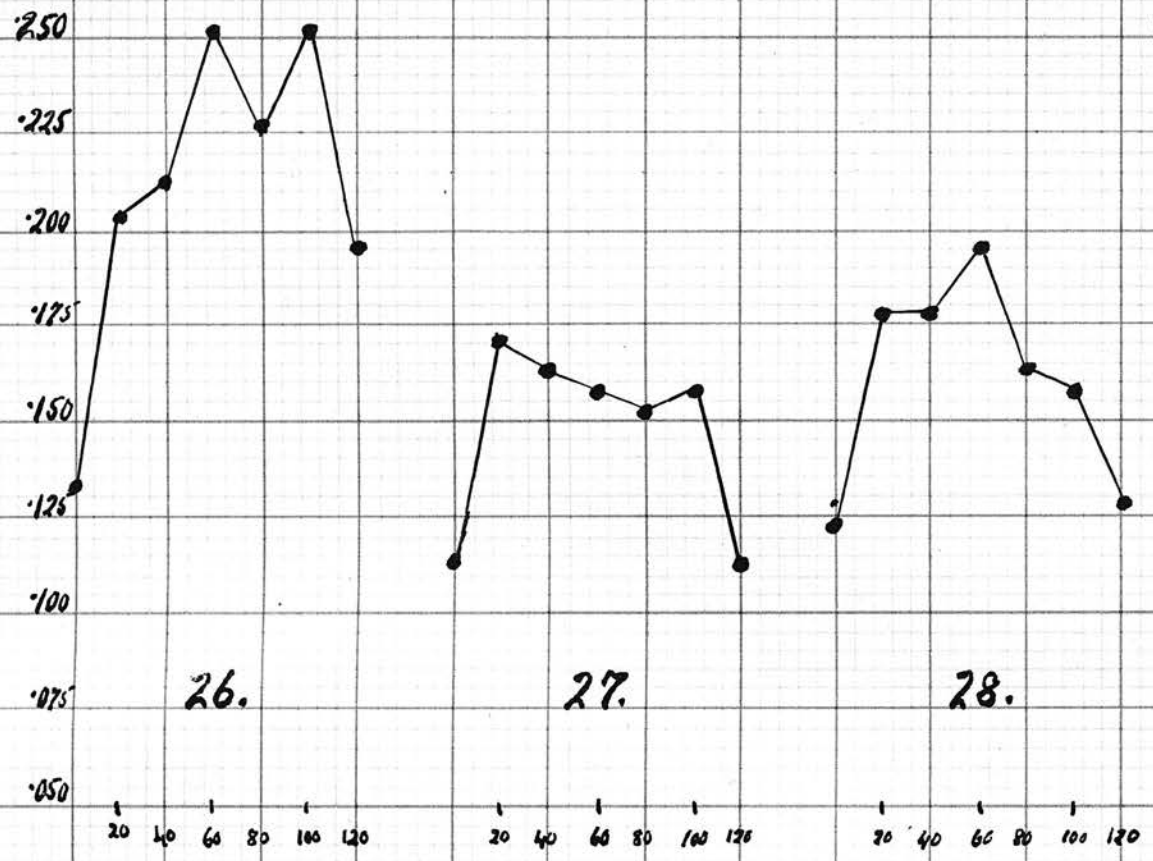
KATATONIA (50 gm. Glucose) (Male)

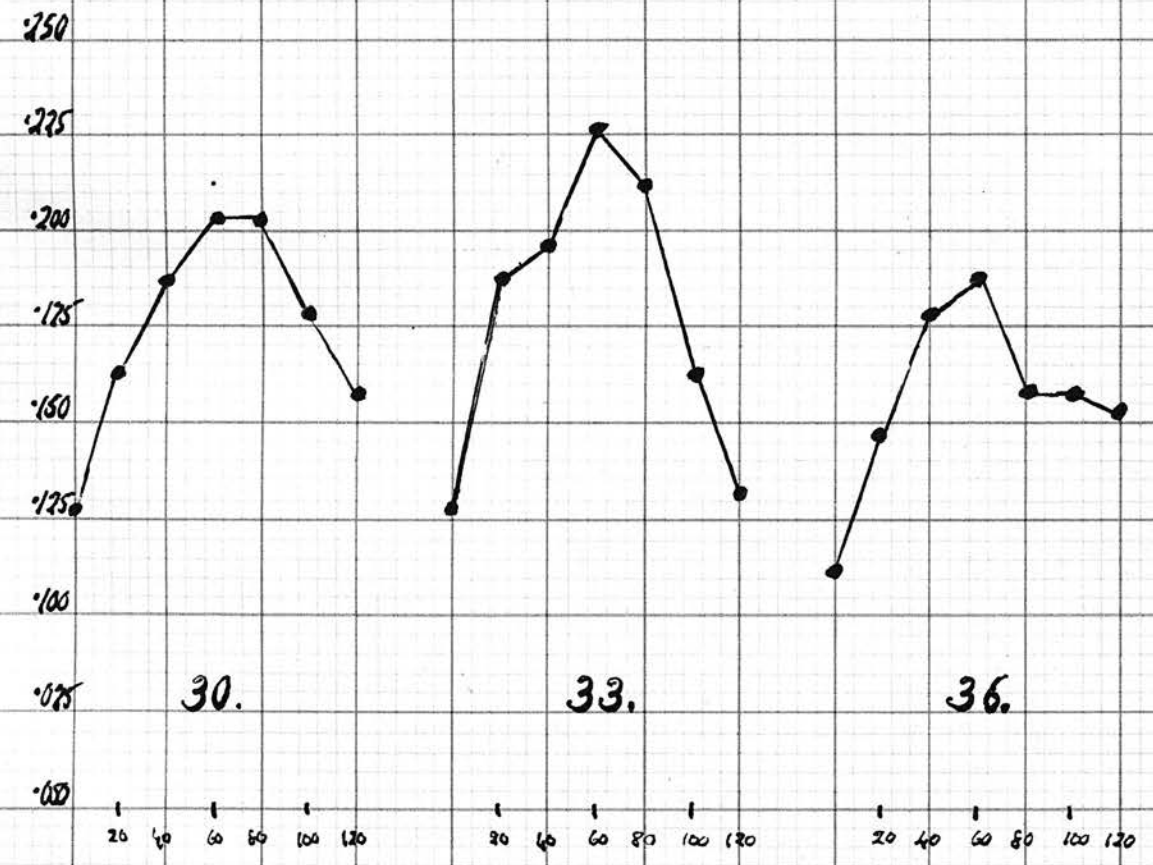
Case	(26)	(27)	(28)	(29)
	1.7.25	1.7.25	3.7.25	3.7.25
	0.132	0.114	0.124	0.105
	0.204	0.171	0.179	0.120
	0.213	0.164	0.179	0.164
	0.252	0.158	0.196	0.196
	0.226	0.152	0.164	0.128
	0.252	0.158	0.158	0.124
	0.196	0.114	0.128	0.097

Case	(30)	(31)	(32)	(33)
	8.7.25	8.7.25	9.7.25	2.8.25
	0.128	0.120	0.117	0.128
	0.164	0.138	0.171	0.187
	0.187	0.158	0.204	0.196
	0.204	0.204	0.204	0.226
	0.204	0.179	0.196	0.213
	0.179	0.164	0.196	0.164
	0.158	0.109	0.164	0.132

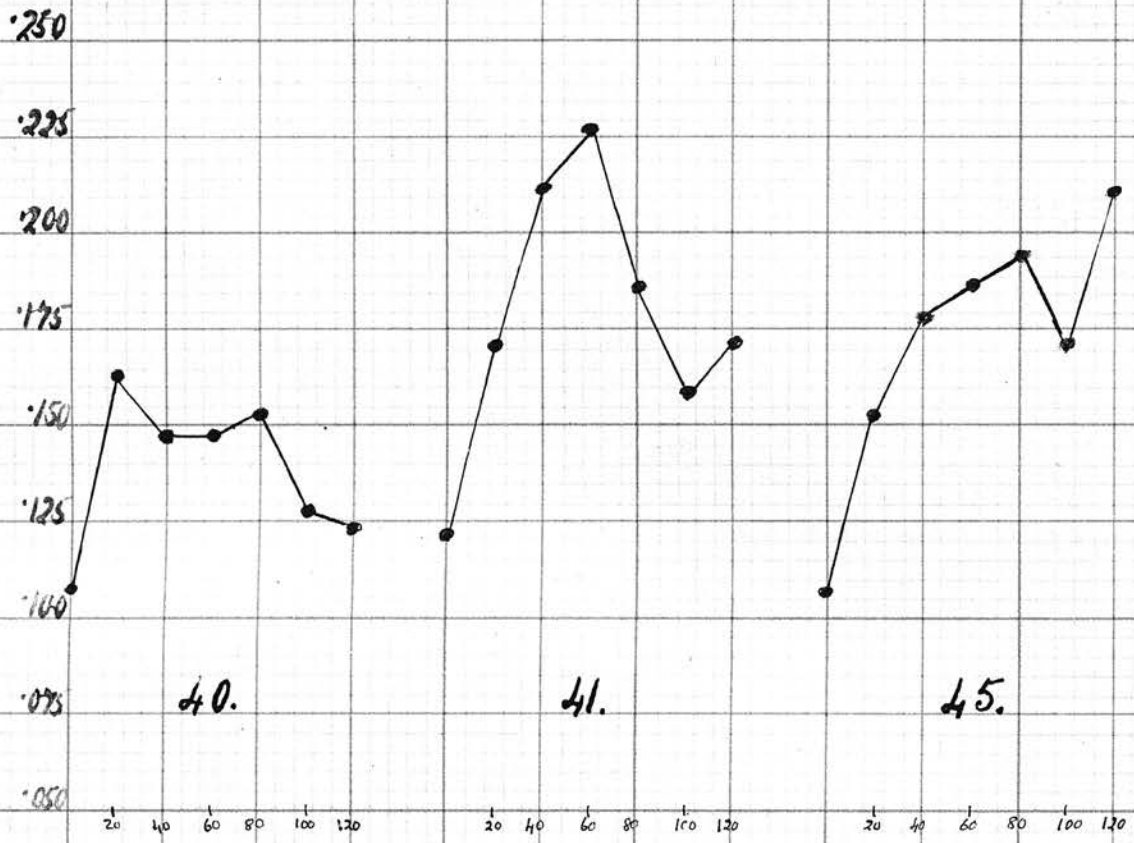
Case	(34)	(35)	(36)	(37)
	30.7.25	29.7.25	30.7.25	13.7.25
	0.120	0.107	0.114	0.105
	0.171	0.124	0.147	0.147
	0.226	0.152	0.179	X
	0.158	0.138	0.187	0.196
	0.164	0.120	0.158	0.147
	0.164	0.124	0.158	0.142
	0.147	0.132	0.152	0.138

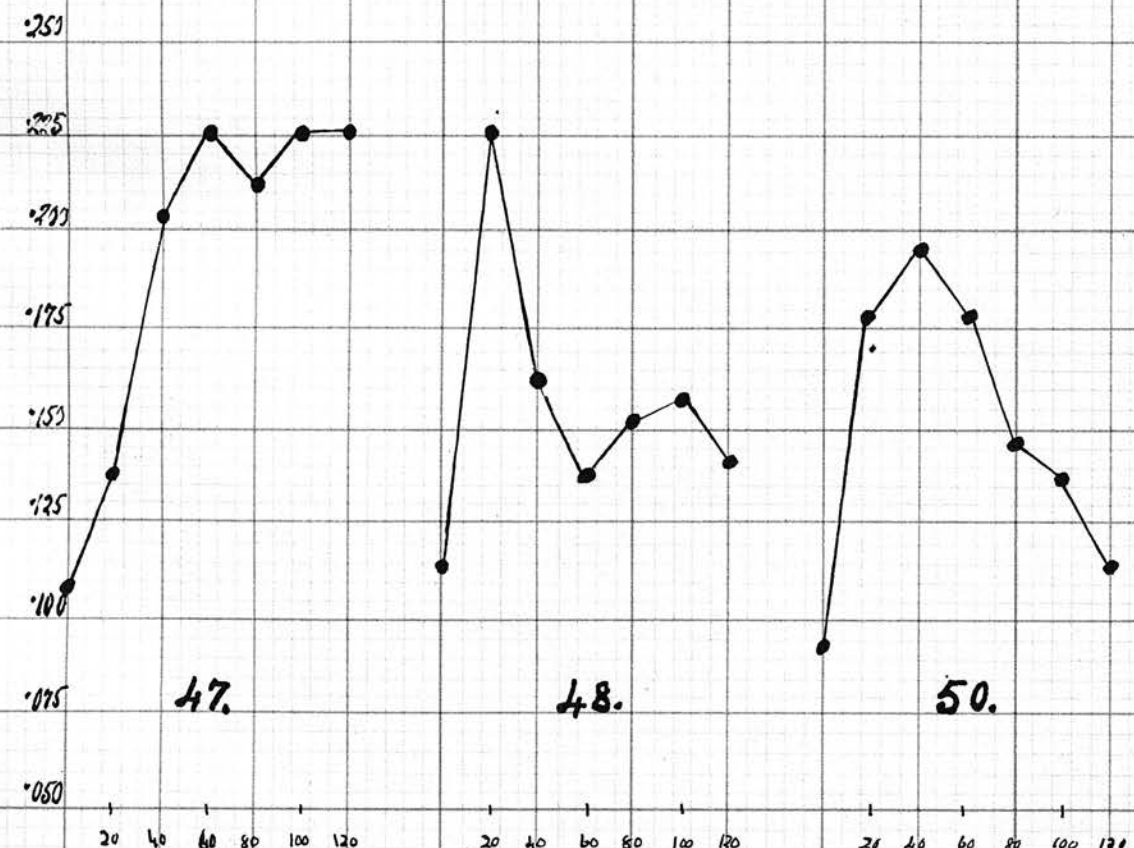
Case	(38)	(39)	(40)	(41)
	13.7.25	17.7.25	17.7.25	18.7.25
	0.111	0.117	0.109	0.120
	0.132	0.152	0.164	0.171
	0.147	0.158	0.147	0.213
	0.158	0.187	0.147	0.226
	0.187	0.171	0.152	0.187
	0.179	0.164	0.128	0.158
	0.171	0.147	0.124	0.171





KATATONIA (50 gm. Glucose) (Female)





KATATONIA · (50 gm. Glucose) (Female)

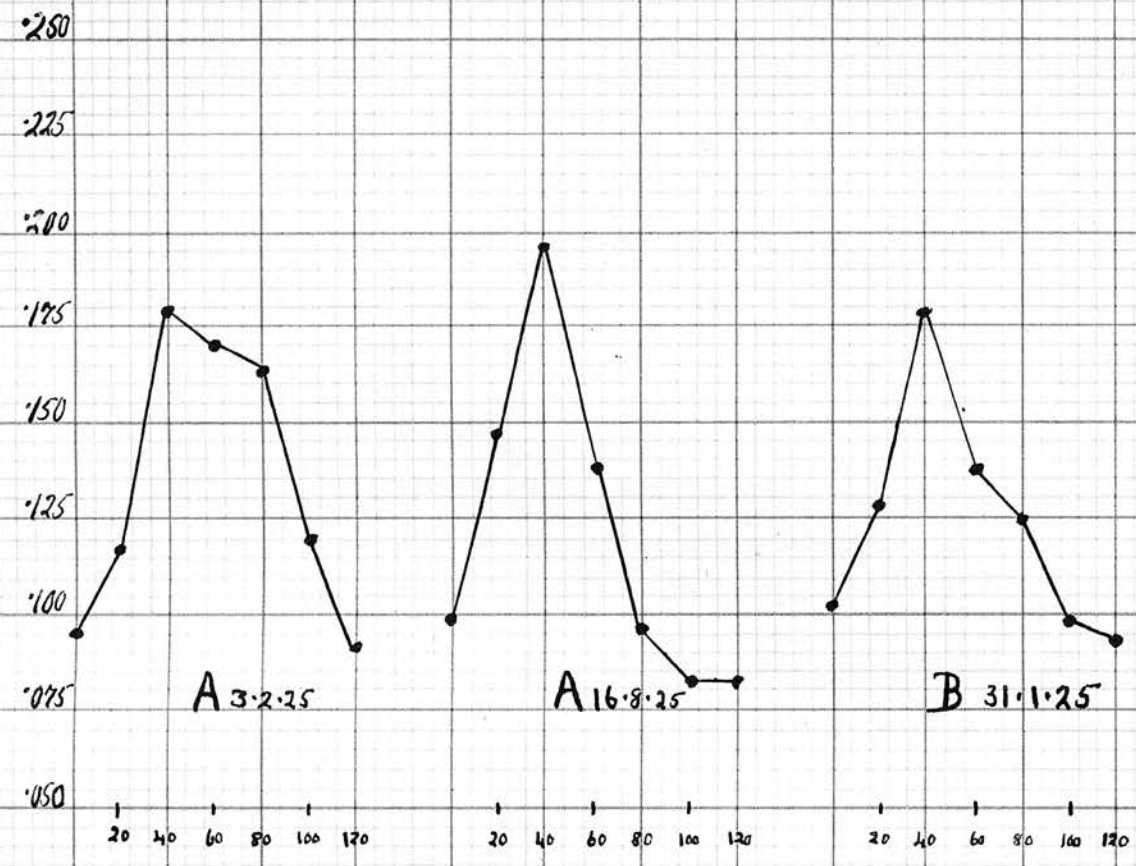
Case	(42)	(43)	(44)	(45)
	22.7.25	22.7.25	23.7.25	24.7.25
	0.124	0.124	0.117	0.107
	0.152	0.128	0.158	0.152
	0.171	0.204	0.187	0.179
	0.179	0.164	0.196	0.187
	0.152	0.152	0.179	0.196
	0.142	0.158	0.158	0.171
	0.111	0.114	0.120	0.213

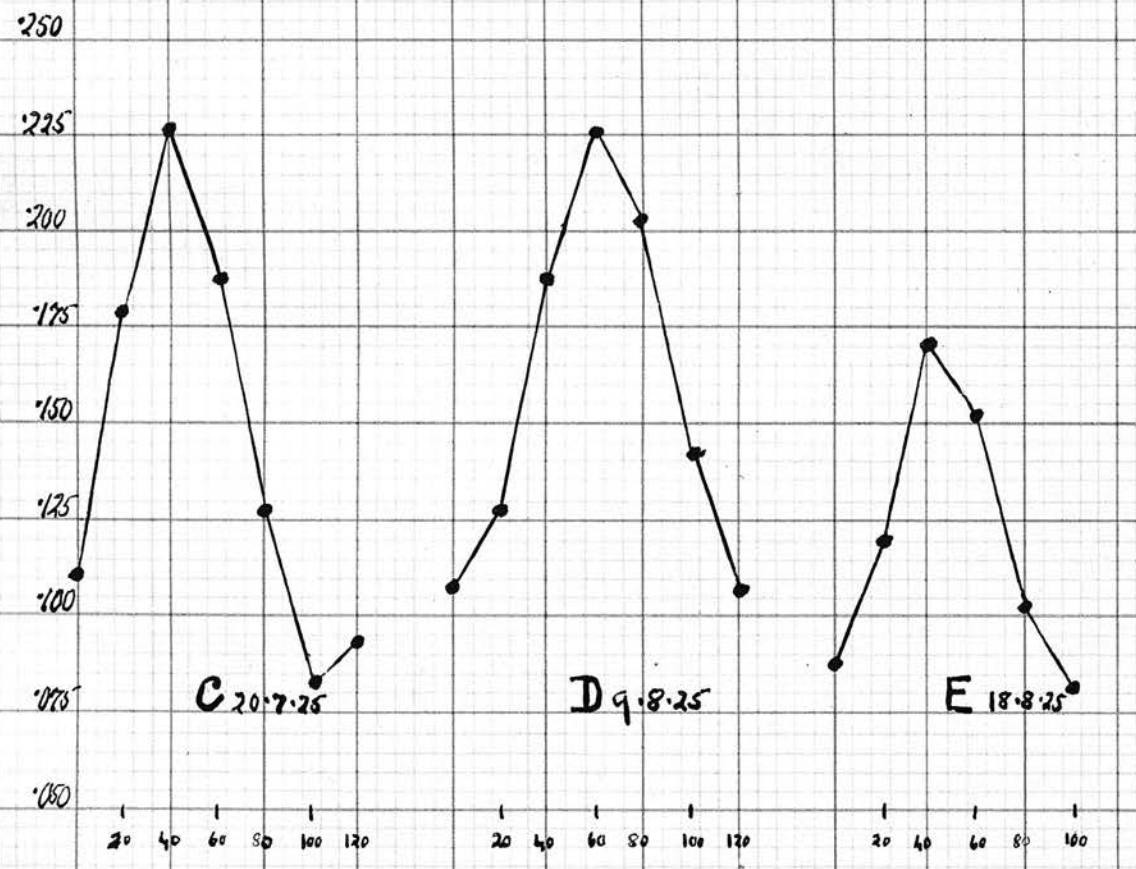
Case	(46)	(47)	(48)	(49)
	24.7.25	27.7.25	27.7.25	29.7.25
	0.109	0.109	0.114	0.120
	0.142	0.138	0.226	0.147
	0.171	0.204	0.164	0.171
	0.147	0.226	0.138	0.164
	0.164	0.213	0.152	0.158
	0.128	0.226	0.158	0.158
	0.079	0.226	0.142	0.158

Case	(50)
	31.7.25
	0.094
	0.179
	0.196
	0.179
	0.147
	0.138
	0.111

Cases 15, 16, 17, 18, 19, 20 and 21 were repeated. Case 20 was repeated on account of the hyper glycaemia shown by his blood sugar fasting level. The other cases were repeated as they were done in one month (February) and with the exception of 18 and 19 showed a much lower curve than the others.

(a)





NORMAL (50 gm. glucose)

The results have been expressed in graphs and these are numbered according to the case. They are grouped on the sheets into Katatonics and Hebephrenics. Where a graph has been repeated it is shown in red.

NORMALS

I have done the sugar test on five normals under the same conditions as the patients.

A.	A.	B.	C.
3.2.25	16.8.25	31.3.25	20.7.25
0.097	0.099	0.105	0.111
0.117	0.147	0.128	0.174
0.179	0.196	0.179	0.226
0.171	0.138	0.138	0.187
0.164	0.097	0.128	0.128
0.120	0.083	0.099	0.084
0.094	0.084	0.094	0.094

D.	E.	A. (3 hours after meals)
9.8.25	18.8.25	3.8.25
0.109	0.089	0.100
0.128	0.120	0.187
0.187	0.171	0.158
0.226	0.152	0.097
0.204	0.102	0.087
0.142	0.081	0.090
0.107		

None of the cases nor any of the normals gave glycosuria or ketone bodies in the urine. Case 6 was not examined as urine was not obtainable owing to his faulty habits.

The Normal Curve.

De Wesselow (7) and McLean (8) state that after the ingestion of 50 gm. Glucose the blood sugar increases to 0.15 to 0.18, this height being attained between 30 and 60 minutes. Then it immediately begins to fall and reaches its original level in about 1½ to 2 hours.

De Wesselow (7) also says that some individuals show a curve rising rapidly to 0.23 in 30 minutes and reaching the original level in 1½ to 2 hours. These cases showed alimentary glycosuria.

Spence (9) investigating infants, found they gave a lower curve than the adult and in five cases from 62 to 75 years of age found four to show high levels and sustained hyperglycaemia after two hours.

McLean (8) states in relation to the renal threshold, that the kidneys do not begin to excrete sugar until the blood sugar is somewhat in excess of 0.17, and that this threshold varies in individuals, but the great majority of people have glycosuria in the region of 0.2%.

Mann (5) employing Calvert's technique, examined 14 normals; the maximum blood sugar varied from 0.150 to 0.210% and a constant return to below the original fasting level in 90 minutes to two hours was found. There was no glycosuria.

Blood sugar values tend to vary with the

preceding diet; a previous diet rich in carbohydrates will give low results, and rich in fat, high results.

The Normal Fasting Level

Hansen (10) by taking blood at 3 minutes interval demonstrated that the blood sugar level is continually fluctuating.

The normal fasting level is in the vicinity of 0.1%. Bowman (1) gives as high a figure as 0.120 and De Wesselow (7) as low a limit as 0.070.

Criteria of Normality.

Fasting Level.

The five normals examined gave fasting levels between 0.089 and 0.111.

Ascent.

As mentioned above the normal curve reaches its peak in 30-60 minutes. In the five normals given they all reach their peak in 40 minutes with the exception of one test (A) carried out when not in bed, which reached the peak in 20 minutes.

Any curve that takes 80 minutes or over to reach its peak is delayed in its ascent.

Peak.

After the ingestion of 50 gm. glucose the

usual peak is 0.15 to 0.18 v.s., but de Wesselow (7) admits to curves where the peak is as high as 0.23 after taking 50 gm. of glucose followed by alimentary glycosuria, while McLean (8) says the renal threshold may be in the vicinity of 0.2%. Mann(5) had normals as high as 0.21%. The duration of these curves above 0.2 is of short duration shown by one sample only at 20 minutes interval. Any curve that keeps above 0.210 for more than 20 minutes will be taken as abnormal.

Descent.

Investigators, (5), (7), (8), (10), into the normal blood sugar appear to be agreed that a failure to return to the vicinity of the original fasting level within 2 hours is abnormal. The usual period for this return is about 90 minutes.

The Blood Sugar Curves in Dementia Praecox.

The 50 cases examined appear to fall into the following groups :-

(1) Normal curves which fulfil the criteria of normality as given above.

(2) Curves rising to over 0.213 and failing to return to the original level within 2 hours, (high delayed return curves).

(3) Curves rising to a level within normal limits (0.158 to 0.213) and failing to return within two hours, (normal peak delayed return curves).

(4) Curves rising to a level below 0.158 and may or may not return to original level in two hours, (low curves).

For purposes of comparison, the following four tables have been drawn up.

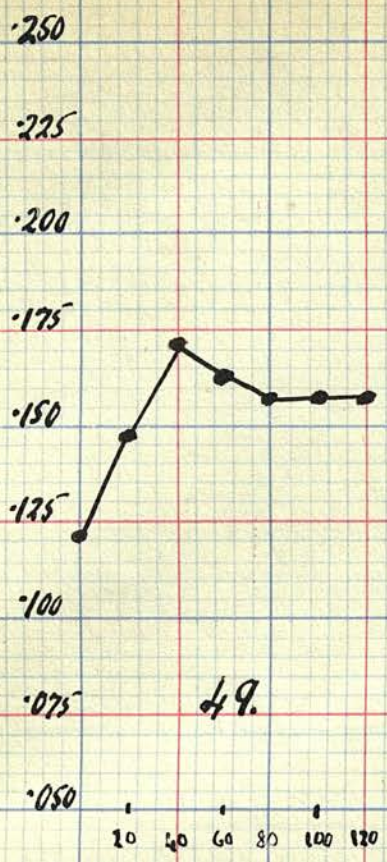
Table 1 gives the subdivision of Dementia Praecox and the sex with the number of cases falling under these headings, grouped according to the type of curve.

Table 11 groups the types of curves they fall into, according to the psychomotor activity they displayed at the time of examination.

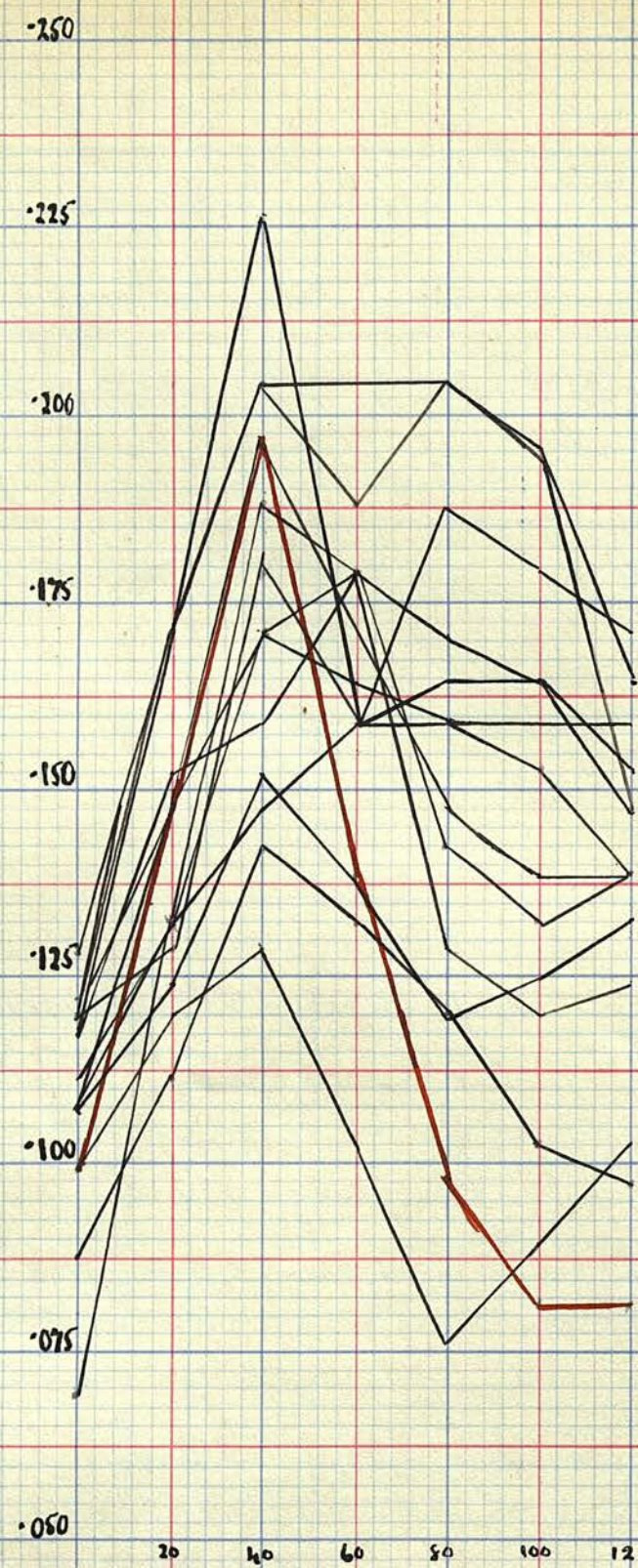
Table 111 shows the relation between duration of the disorder and the type of curve. The duration is taken as short if it falls under two years. The remaining groups of the table of cases (see p.) are considered as long. The duration is dated from the date of onset as observed by the relatives and not from the date of admission into the hospital.

Table 1V compares the ages of the patients and the type of case.

(g)



HEBEPHRENIA
(Female)
50 gm. Glucose.



High Delayed Return (Group II)

·213

Normal Peak Delayed Return (Group III)

·158

Low Curves. (Group IV)

Average Normal Curve in Red.

HEBEPHRENIA.
Abnormal Blood Sugar Curves (superimposed)

(N.B. Note majority in group 3)

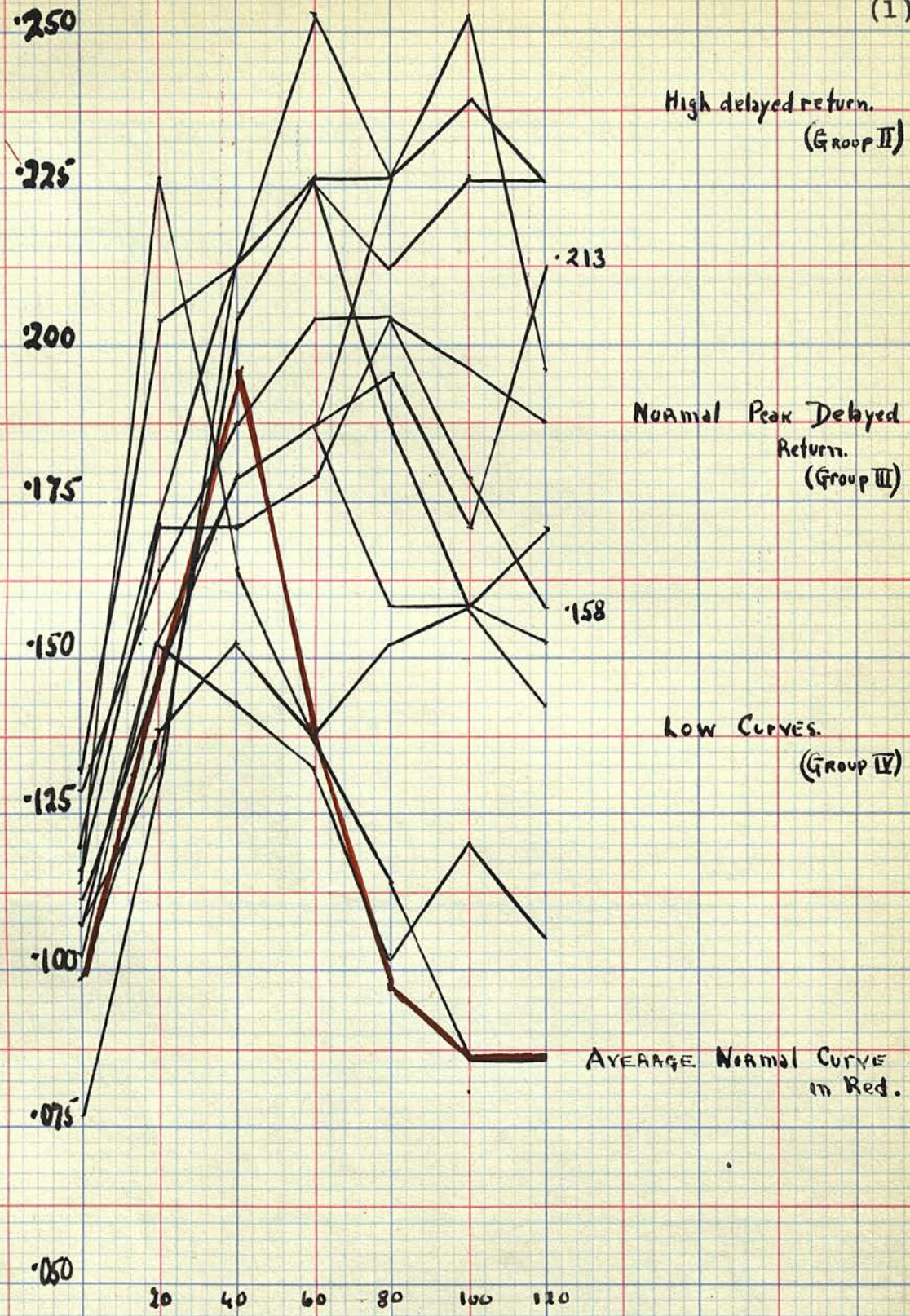
Table 1

Curve group.	Hebephrenia.			Katatonia.		
	Male.	Female.	Total.	Male.	Female.	Total.
1.	7	6	13	5	3	8
2.	0	1	1	1	4	5
3.	5	5	10	1	5	6
4.	3	1	4	3	0	3
	15	13	28	10	12	22

From this table it can be seen that out of 50 cases of Dementia Praecox, 29 present abnormalities, and that the greatest number of these is in the category whose curve has a normal peak with delayed return to normal.

In comparing Hebephrenia with Katatonia it is evident that the latter has a greater number of high delayed return to normal curves in the proportion of 1:28 to 5:22. The remaining abnormal types are equally represented. The total abnormal cases in Katatonia is greater than in Hebephrenia in the proportion of 14:22 to 15:28.

With regard to sex, the female shows a slightly greater proportion in 16:25 to 13:25 abnormal curves. While in the types of abnormal curves there is a



KATATONIA.
(Abnormal Blood Sugar Curves (superimposed)
(N.B. Note majority in group 2 and 3)

preponderance of high delayed curves in the female of 5:1 over the male, and of 10:6 in the normal peak with delayed return. The male curves are greater than the female in the low curves in the proportion of 6:1.

Table 11.

Curve group.	Stuporose.	Excited.	Neither.
1.	11	4	6
2.	5	1	0
3.	7	5	4
4.	3	2	2
	26	12	12

The main feature from this table is the greater number of cases of stupor appearing in the curve of high delayed return to normal type, in the proportion 5:26, 1:12 and 1:12.

There is also a slighly greater proportion of abnormal curves in the cases showing psychomotor abnormalities than in those showing none.

Table 111.

Curve group.	Duration. Short.	Long.
1.	11	10
2.	1	5
3.	10	6
4.	2	5
	24	26

The above table shows a greater proportion of high delayed return curves (group 2) in the cases of long duration over those of short.

Table 1V.

Curve group.	Age Under 25 years.	25 Years and over.
1.	9	12
2.	2	4
3.	9	7
4.	3	4
	23	27

From the above table the age incidence does not appear to influence the abnormality of the sugar curve.

Fasting Level.

The following table gives the abnormal fasting levels in relation to the type of Dementia Praecox.

	Over 0.120	Under 0.080
Hebephrenia	4	1
Katatonia	5	1

This shows only 7:50 abnormal fasting levels, the majority of which are above the normal level.

Repeated Curves.

Several cases were repeated, 15, 16, 17, 18, 19, 21 and Normal A. in the summer (v. red graphs on graph sheets

Of these cases 17, 18 and 21 gave curves of a type different to the preceding one. The normal curve gave a higher one. The normal is not a constant but still fulfills the criteria of normality while the Dementia Praecox shows considerable variation.

Significance of the Blood Sugar Curve.

It is generally accepted that the rise in the concentration of the blood sugar following the ingestion of sugar represents the absorption of the sugar via the portal vein. The arrest of the ascent

and subsequent rapid fall involves more factors. That it is not due to the cessation of absorption the following facts are found.

The diabetic curve continues to rise beyond the normal period (30 to 60 minutes), showing that absorption is continuing (8); and that one hour after the ingestion of a sugar meal 18 to 66% of the original can be recovered from the stomach while the blood sugar curve is falling (7). That the sugar is eliminated from the body via the kidneys is excluded by the absence of glycosuria. There remains the elimination by oxidation or the intervention of some storage mechanism. An increase in the respiratory quotient is found at the time when the curve is falling which continues for some time after but only accounts for 18% of the sugar ingested; nor is the increased metabolism proportional to the glucose taken. Therefore it is maintained that the oxidation of the blood sugar is not the sole factor in the fall of the curve. The remaining factor is the action of some storage mechanism. This mechanism is the conversion of glucose to glycogen and this glycogenesis is divided between the muscles and the liver; the relative parts played by these is not known (7).

The Blood Sugar Curve in Dementia Praecox.

From the grouping of the 50 curves, the following

is a summary of the conclusions arrived at :-

(1) That there is no type of blood sugar curve pathognomic of Dementia Praecox.

(2) That in Dementia Praecox there is defective glycogenesis which appears to be slightly more evident in katatonia than in hebephrenia, and that this abnormality is more evident in the female sex.

(3) That the low curve is more common in the male sex, (also observed by Drury & Farran Ridge (4).

(4) That defective glycogenesis is more evident in the cases of long duration and a high level more frequent in these cases.

(5) Age does not influence the incidence of abnormal curves in Dementia Praecox.

(6) There is evidence of defective glycogenesis in stupor.

Some Observations on Individual Curves.

There are certain curves which, while falling into the groups above mentioned, are of special interest.

These are the curves from cases 6, 18, 20, 26, 45 and 7.

Case 6 was one of stupor, anergic in type following an attack of acute katatonic excitement.

Other factors that could bear on this abnormal curve besides the profound stupor are diet, as he had been fed on a milk diet for six weeks before. Previous diets rich in fat tend to yield high results.

Case 18 is of interest in that although the two curves are widely different in values there was no apparent difference in the patient's mental state, (hebephrenic excitement).

Case 20 is interesting because of the hyperglycaemia shown and also that with this initial hyperglycaemia the further rise after ingestion of 50 gm. of glucose is not greater; there was no glycosuria. The case was one of hebephrenic excitement but he also showed dilated pupils, flushed face and tachycardia, suggesting sympatheticotonia. The hyperglycaemia would be in keeping with such a condition.

Case 26 is a similar curve to Case 6, and the stupor was as profound but not anergic; she was slightly resistive.

Cases 45 and 7 are curves showing delayed ascent such as would be suggestive of faulty absorption but also show a high level at the end of two hours.

It will be noticed from the first list of cases that all curves of katatonia are from stuporose cases with the exception of cases 40 and 50 which were excited; these curves do not present high curves.

It might appear probable than that the conclusions drawn from katatonia are dependent on the stupor.

Commentary.

Technique.

The fallacy of the technique is 5% and an allowance of three times this (0.015) does not affect the conclusions except those in group 4 (low curves) which could be raised to the normal limits by addition of 0.015.

The low curve, says de Wesselow (7), should not have too much emphasis laid on it as it may merely mean a poor absorption and the general shape of the curve is of more significance than the level of its apex.

The facts that arise to be discussed are the defective glycogenesis and in some cases the defective absorption in Dementia Praecox. The latter fact can be more readily understood as it is well known that the alimentary tract in mental disorders requires continual attention and treatment.

The question of glycogenesis is more difficult owing to the imperfect knowledge of this mechanism in the normal. The process of glycogenesis in the liver is not impaired in Dementia Praecox, assuming the laevulose glycaemia reaction test an adequate one, Mann (7).

Is there any evidence of impairment of glyco-

-genesis in the systematic blood? The factor in this is the pancreas and the question arises - Is there any pancreatic deficiency in Dementia Praecox? The injection of insulin reduces these high sustained curves (Drury & Farran Ridge (4)) occurring in Confusional Insanity.

The character of the abnormal curve found in Dementia Praecox is analogous to that of the diabetic, with the exception that there is rarely an initial hyperglycaemia and frequently the descent of the Praecox curve is sudden and not the gradual one of diabetes.

Lovell (11) infers that the functional impairment of the pancreas in early anxiety psychoses may later lead to permanent damage. It is of interest then to note the greater proportion of high sustained curves in cases of long duration in the 50 cases examined for this thesis, which would be in keeping with progressive impairment of the mechanism for glycogenesis, (Table 111). Drury & Farran Ridge (4) state that acute cases give higher curves than chronic.

The cause of defective glycogenesis in diabetes is accepted as deficiency in the pancreatic internal secretion insulin; in mental disorder there appears to be more factors to be considered.

Mann (5) summarising the cause of sustained hyperglycaemia in relation to the work of Langfeldt

states that it may be due to inhibition of glycogenesis due to endocrine hyperactivity, excessive diastase activity due to the same cause or change in the p.H. of the liver, and to pancreatic inefficiency. His results from investigation along these lines are that if there were no obvious endocrine disorder the results did not justify the abnormalities being attributed to endocrine activity and that the liver seemed to be absolved from blame. He infers that the defective storage is due to changes in the ionic state of the organism depressing pancreatic function. The general conclusion being that the defective glycogenesis is but one example of disordered metabolism.

Action of Endocrine Glands on the Blood Sugar.

In the preceding commentary, reference has been made to the influence of the endocrine glands on sugar metabolism.

The following is a brief summary of the activity of the endocrine glands in relation to the blood sugar.

Thyroid Gland.

In Graves disease there is as high a percentage of glycosuria as 60%; the blood sugar curve is higher and more prolonged and normal, and the renal threshold and fasting level are normal. As there

is double the proportion of glucose oxidised, the defect in tolerance must be in storage (Sanger & Hun). (12). Cramer found that administration of thyroid depletes the liver glycogen. Administration of thyroid leads to a similar type of curve and glycosuria.

Adrenal Glands.

The injection of the adrenalin leads to hyperglycaemia through glycolysis of the liver glycogen. There is evidence of antagonistic reactions between the adrenals and the pancreas, viz., neither puncture diabetes nor pancreatic occur after extirpation of the adrenals and Loew's eye test for dilatation of the pupil by adrenalin in the presence of pancreatic disease.

Pituitary.

The injection of posterior lobe of pituitary gland raises the blood sugar and in many cases induces glycosuria, and there is also the raised carbohydrate tolerance in pituitary dysfunction, pointing to a positive action on the part of the pituitary in relation to raising the blood sugar.

Pancreas.

The influence of the pancreatic internal secretion in reducing the blood sugar is well known; the discovery of insulin and its source from the islet tissue being established.

The adrenals, thyroid and pituitary glands,

therefore, act to increase the blood sugar while the pancreas has the opposite function.

Relation of Sympathetic Nervous System to Endocrine Glands.

Langdon Brown (13) states that the following may be accepted as facts .- "Sympathetic stimulation increases blood sugar as a defensive measure; sympathetic stimulation causes increased secretion of adrenals, thyroid and pituitary. Vagus stimulation excites secretion of the pancreas and it is probable that sympathetic stimulation inhibits the secretion of the pancreas. The general effect of sympathetic stimulation is katabolic and mobilisation of blood sugar is a preparation for katabolic action; therefore the sympathetic would by increasing the secretion of glands which diminish carbohydrate tolerance and by inhibiting the gland which increases carbohydrate tolerance, would raise the blood sugar above the leak point and glycosuria would result".

He suggests as a classification of persistent glycosuria an overaction of adrenal thyroid pituitary or underaction of pancreas forming an organic orogin and a sympathetic origin with functional overaction of adrenals, thyroid or pituitary and underaction of pancreas.

The relation between the endocrines and sympathetic nervous system has been mentioned because of the clinical evidence pointing to some disordered action on the part of either or both of these. In mental disorder, such symptoms and signs as tachycardia and cardiac arrhythmia, flushing and sweating particularly of the palms of the hands, dermographia and other vasomotor disorders; also the disorders of muscle tone found particularly in Katatonia.

In Dementia Praecox there has been demonstrated regressive atrophy of the testes and ovaries by Sir F.W.Mott, (14) and also he has found loss of weight in the adrenal glands in this disease. The medullary changes described being increased number of nuclei with irregularities of size and form and a deficiency of chromatin with increased fibrous tissue and fibroblastic nuclei.

To sum up, there is evidence of pathological change in some of the endocrines in Dementia Praecox, (testes and ovaries, adrenals); there is evidence of influence of the endocrines and sympathetic nervous system on the blood sugar: that there is evidence of defective glycogenesis in Dementia Praecox: that there is clinical evidence of faulty action of the sympathetic nervous system in cases of Dementia Praecox particularly Katatonia.

From a consideration of these facts the question arises - Is the defect in the glycogenesis in cases

of Dementia Praecox due to -

(a) Overactivity of the thyroid adrenalin pituitary group of endocrines?

(b) Defective action of the pancreas?

(c) Overactivity of the sympathetic (Sympathetic tonia)?

(d) Defective activity of the para-sympathetic?

(e) Other causes, such as a change in the ionic state of the tissues (vide supra) and in the infective conditions an abnormal sustained hyperglycaemia may result following glucose ingestion (Olmsted & Gay 15).

From the standpoint of the sympathetic endocrine influence on the blood sugar, in the following pages are given the values of the blood sugar curve after injection of sympathomimetic and parasympathomimetic drugs and endocrine extracts, co-incident with the ingestion of 50 gm. glucose.

SECOND PART.

Method.

The conditions under which the tests were carried out were identical with those for the ordinary ingestion curve as given above.

The fasting level sample having been taken the patient was then injected with the drug and then

drank 50 gm. glucose in 150 to 200 c.c. of water. The following were the drugs administered :-

Drug.	Dose.	Method of administration.
Atropine Sulph.	$\frac{1}{50}$ gr.	Hypodermically.
Pilocarpine Mt.	$\frac{1}{10}$ gr.	Hypodermically.
Pituitary Post.Lobe (Infundin Burroughes Welcome).	1 c.c.	Intramuscularly.

Adrenalin 5 minnims were given hypodermically without any ingestion of glucose.

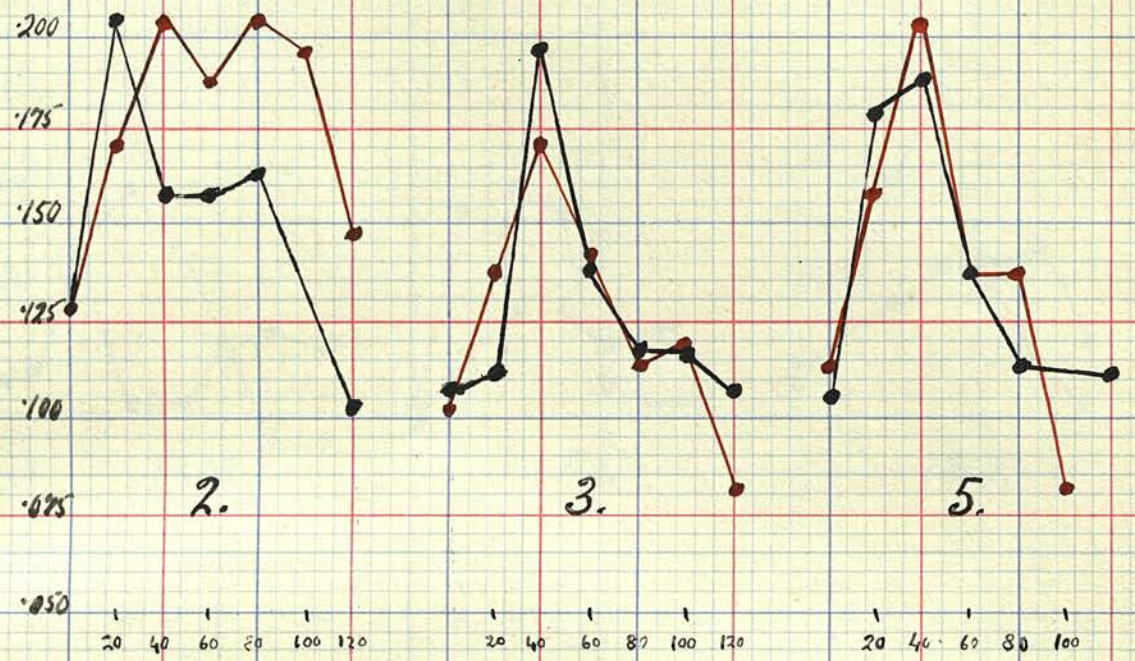
To estimate the influence of thyroid, the patient's blood sugar curve was estimated after ingestion of 50 gm. glucose; that day he took 1 gr. thyroid extract twice a day, the next day 2 gr. twice a day, then 2 gr. three times a day, then 5 gr. twice a day and then 5 gr. three times a day for three days. The blood sugar curve was again estimated on the morning of the eighth day. In two cases the blood sugar curve was estimated at intervals during 14 days they were taking thyroid.

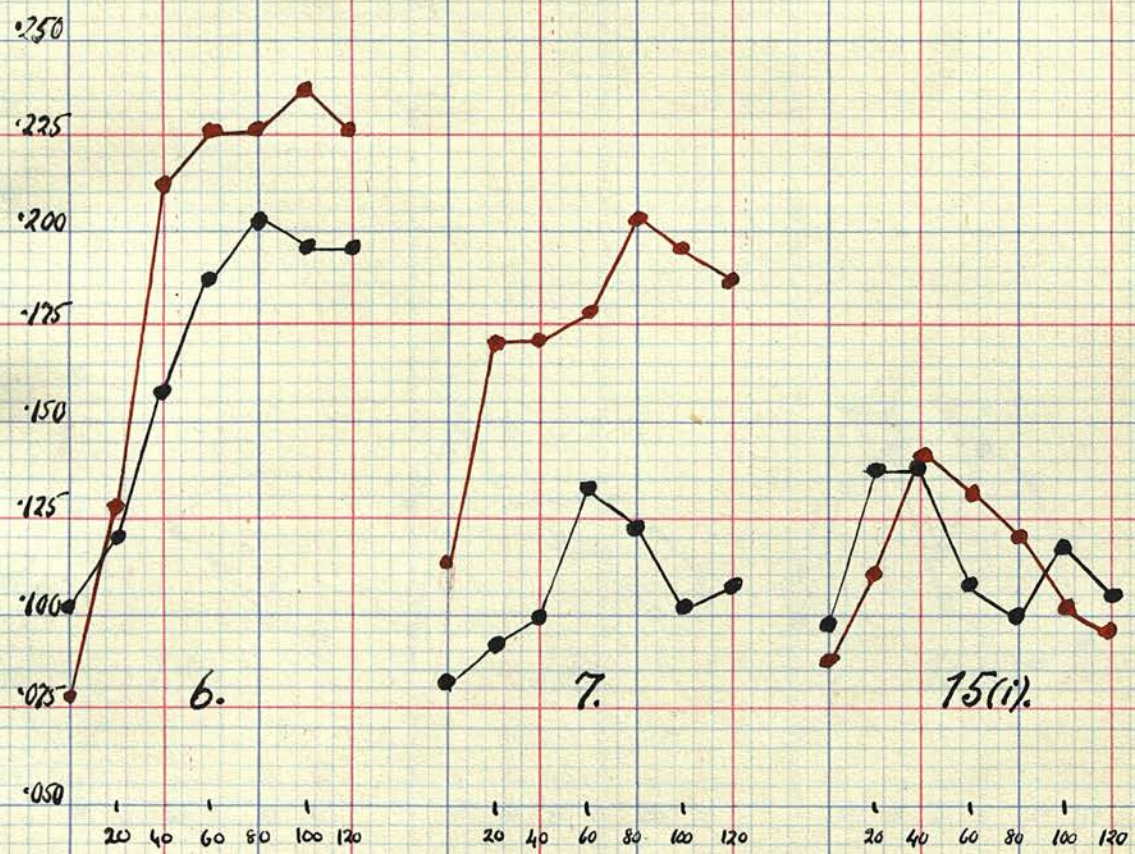
Cases.

The cases selected were 11 of those upon whom the ordinary sugar curve had been estimated.

All the drugs named were administered to these cases, an interval of one week or more being allowed to lapse between the tests. Thus the variations shown as a result of the drug are comparable as they

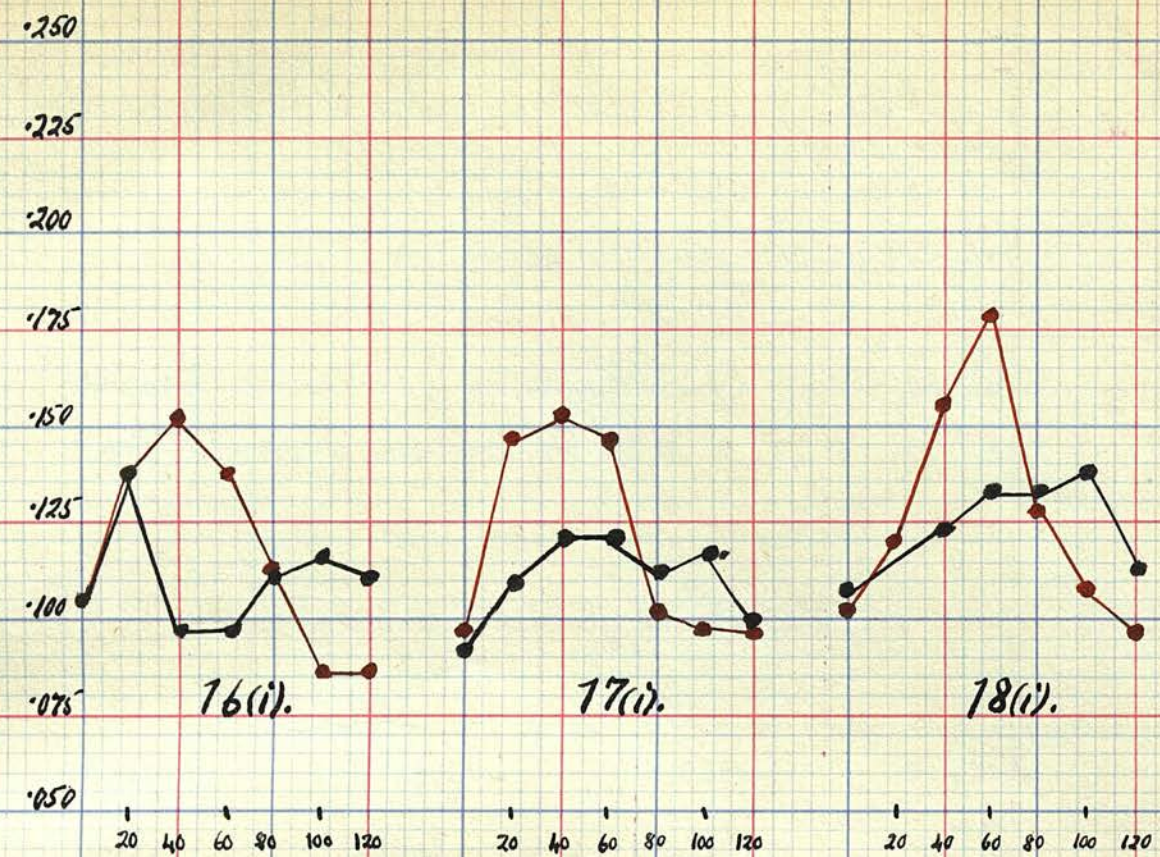
Ordinary blood sugar curves are in red ink, in all subsequent graphs.

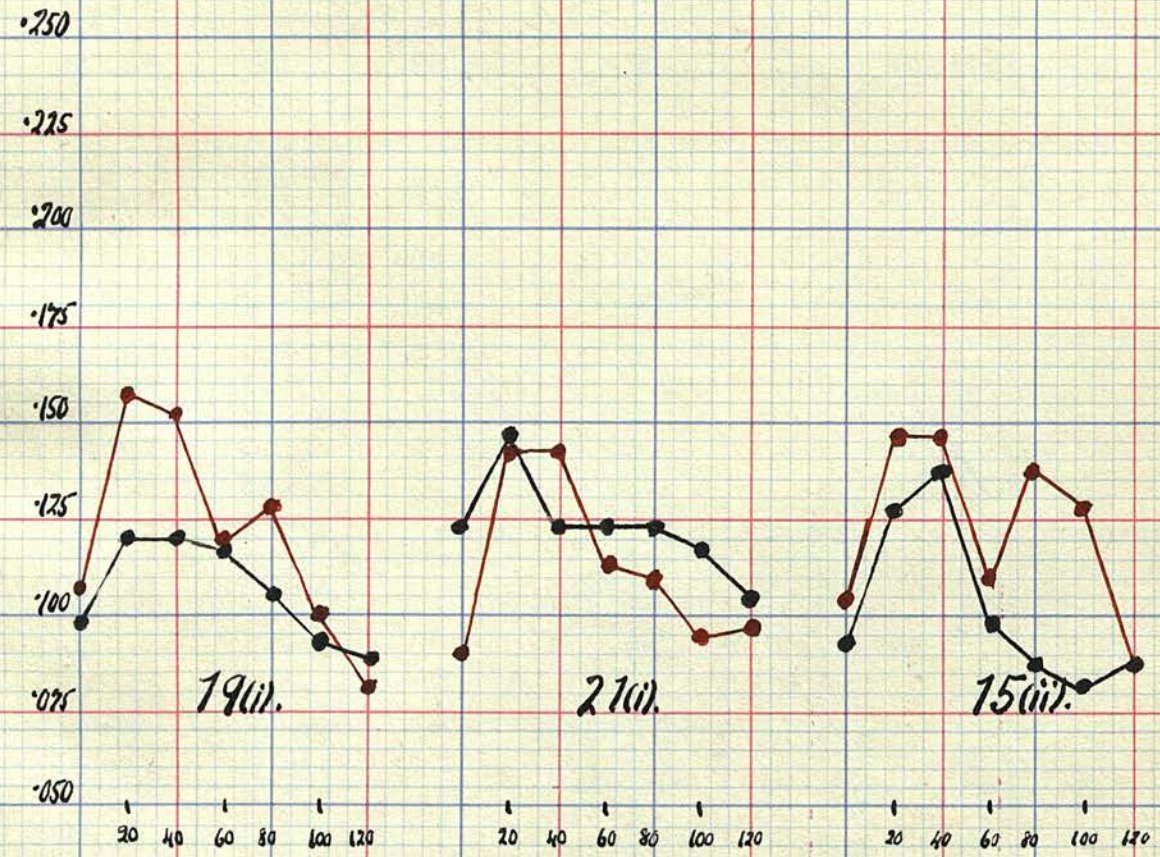




DEMENTIA PRAECOX $\frac{1}{50}$ Atropine Sulph. 50 gm. Glucose.

(n)





DEMENTIA PRAECOX 1/50 Atropine Sulph. 50 gm. Glucose.

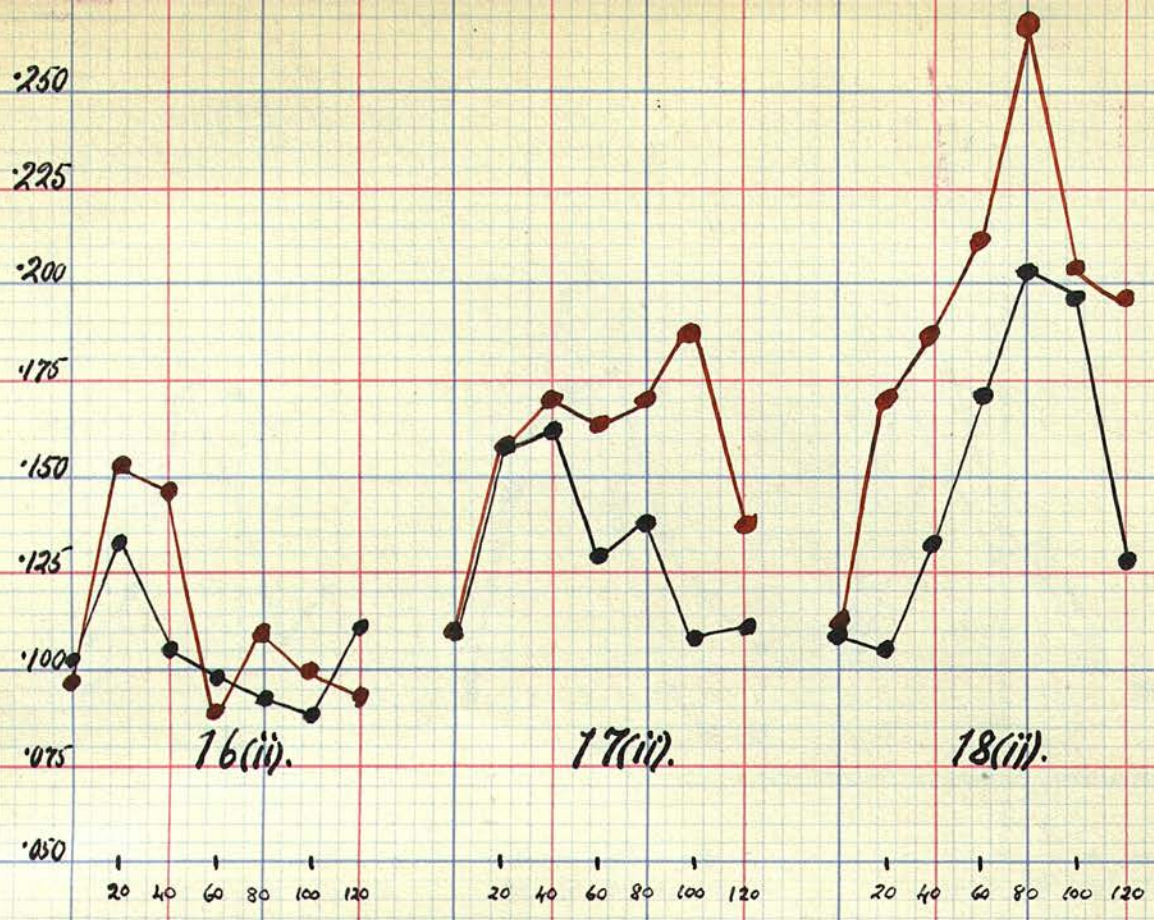
are estimated on the same individual and at about the same time. The cases are regarded as Dementia Praecox without division into Katatonia and Hebephrenia, there being an insufficient number to do so. Their reference numbers are 2, 3, 5, 6, 7, 15, 16, 17, 18, 19 and 21.

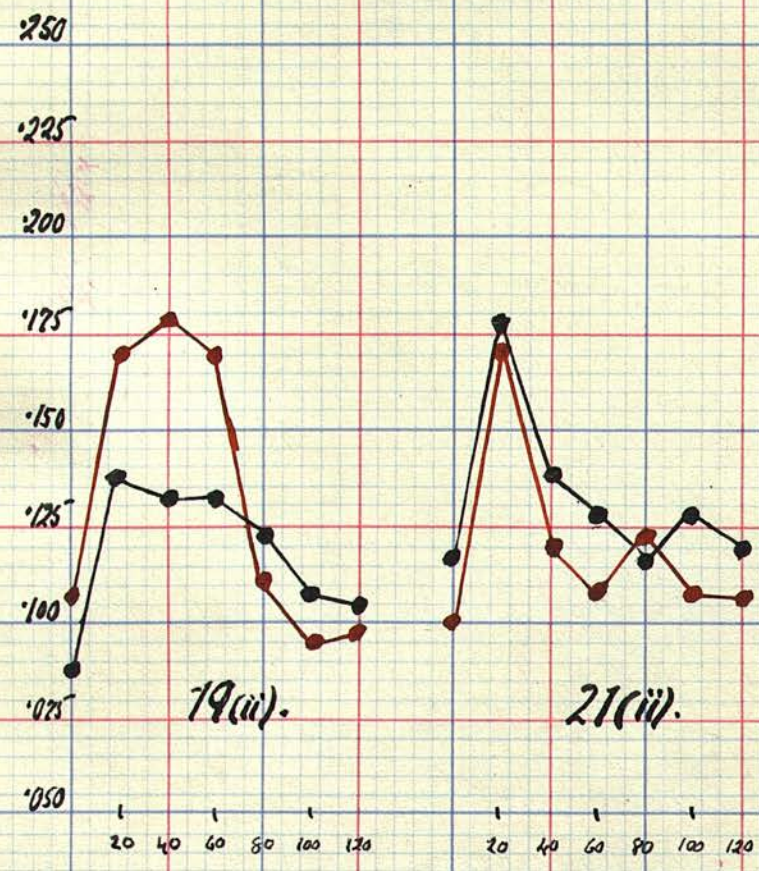
Atropine Sulphate $\frac{1}{50}$ gr. Hypoderm.

(2)	(3)	(5)	(6)
14.1.25	27.1.25	1.2.25	25.1.25
0.128	0.109	0.105	0.102
0.204	0.102	0.179	0.120
0.158	0.196	0.187	0.158
0.158	0.138	0.138	0.187
0.164	0.117	0.114	0.204
X	0.117	X	0.196
0.104	0.108	0.111	0.196

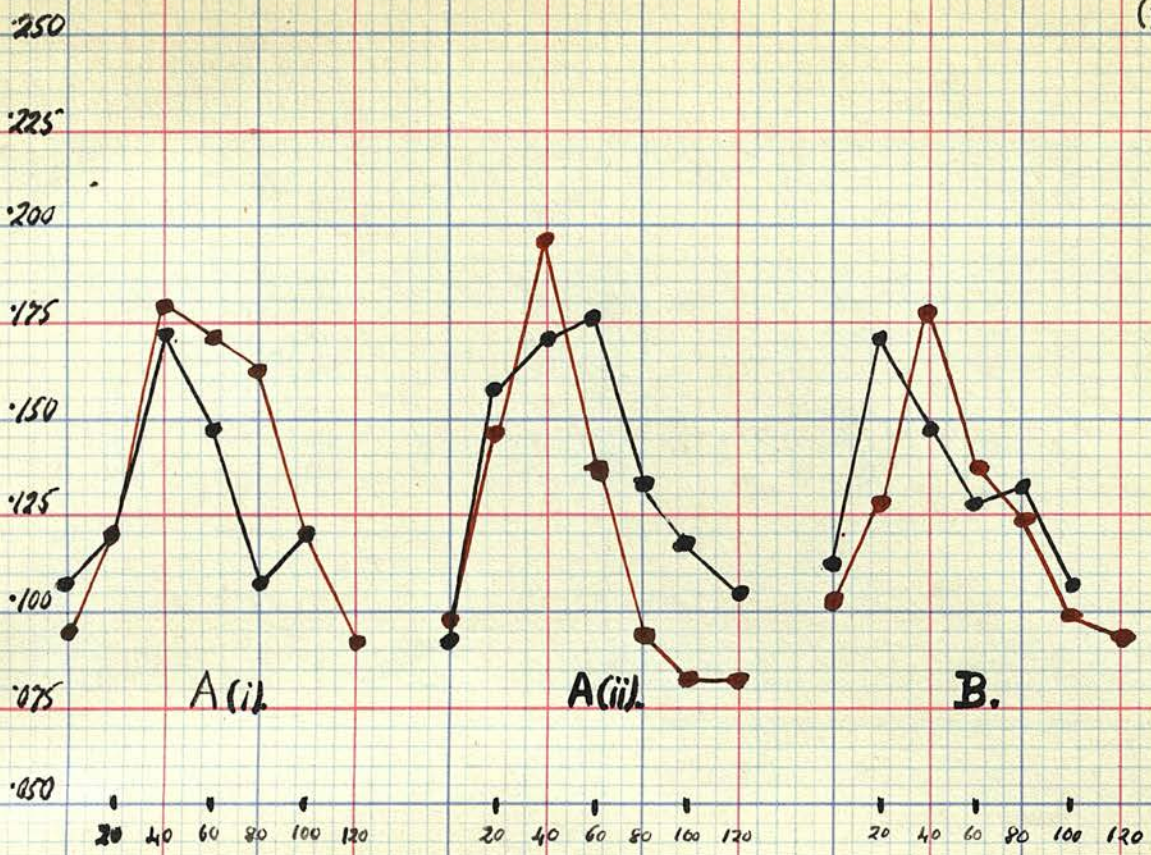
(7)	(15)		(16)	
	(i)	(ii)	(i)	(ii)
30.1.25	4.3.25	14.8.25	4.3.25.	14.8.25
0.081	0.099	0.093	0.105	0.102
0.093	0.138	0.128	0.138	0.132
0.100	0.138	0.138	0.097	0.105
0.132	0.109	0.097	0.097	0.097
0.124	0.100	0.087	0.114	0.093
0.102	0.117	0.081	0.117	0.089
0.109	0.105	0.087	0.111	0.111

(17)		(18)	
(i)	(ii)	(i)	(ii)
1.3.25	11.8.25	1.3.25	11.8.25
0.093	0.114	0.107	0.109
0.111	0.158	X	0.105
0.120	0.164	0.120	0.132
0.120	0.128	0.132	0.171
0.111	0.138	0.132	0.204
0.117	0.109	0.138	0.196
0.097	0.111	0.114	0.128





DEMENTIA PRAECOX $\frac{1}{50}$ Atropine Sulph. 50 gm. Glucose.



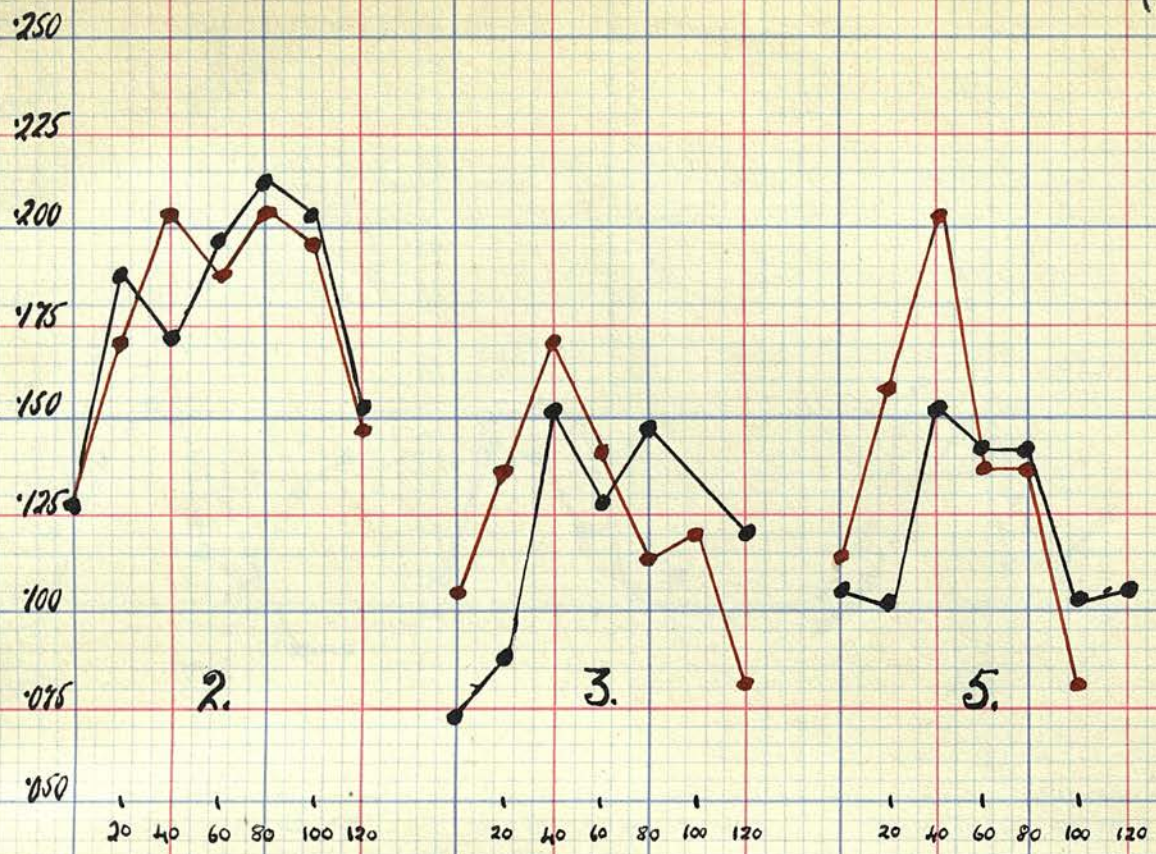
NORMAL $\frac{1}{50}$ Atropine Sulph. 50 gm. Glucose.

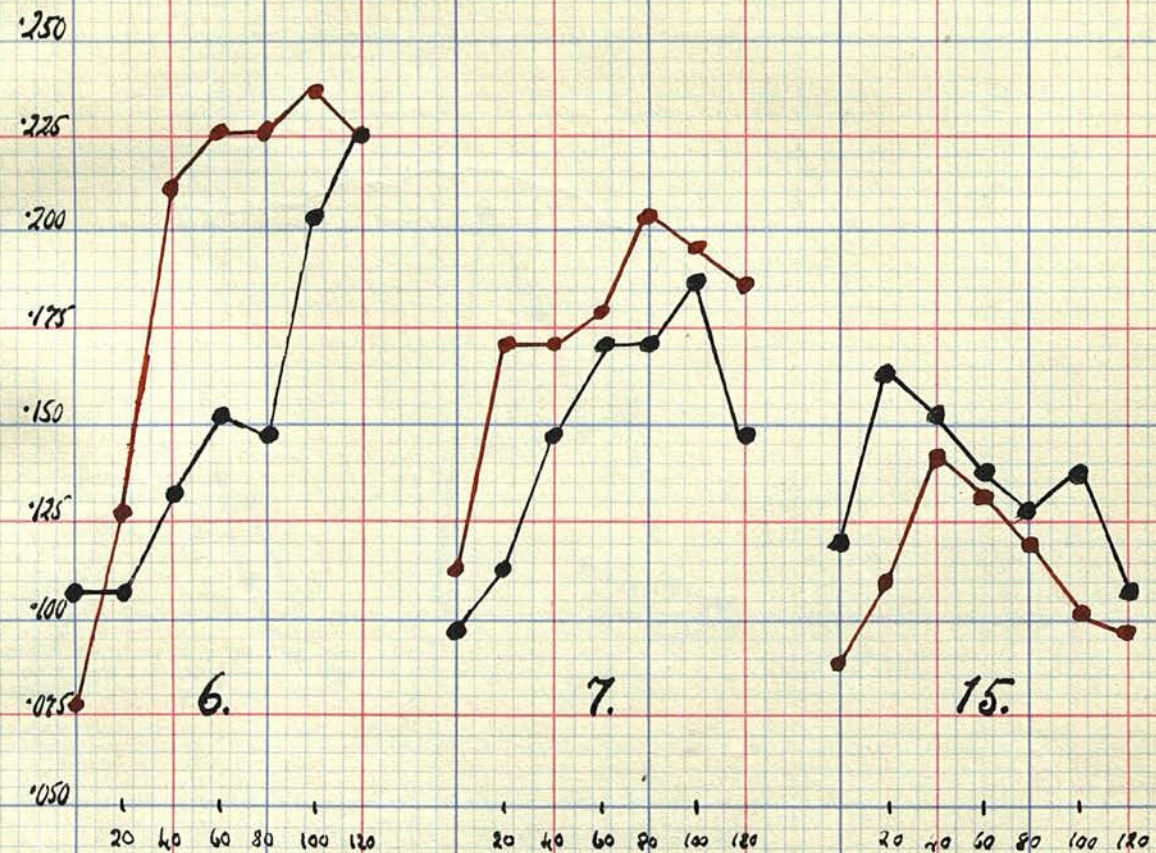
(19)		(21)	
(i)	(ii)	(i)	(ii)
11.3.25	15.8.25	11.3.25	15.8.25
0.099	0.087	0.124	0.117
0.120	0.138	0.147	0.179
0.120	0.132	0.124	0.138
0.117	0.132	0.124	0.128
0.105	0.124	0.124	0.117
0.099	0.109	0.117	0.128
0.089	0.105	X	0.120

A. (Normal).		B. (Normal).
(i)	(ii)	
4.2.25	21.8.25	10.2.25
0.109	0.093	0.114
0.120	0.158	0.171
0.171	0.171	0.147
0.147	0.179	0.128
0.107	0.132	0.138
0.120	0.117	0.109
X	0.105	X

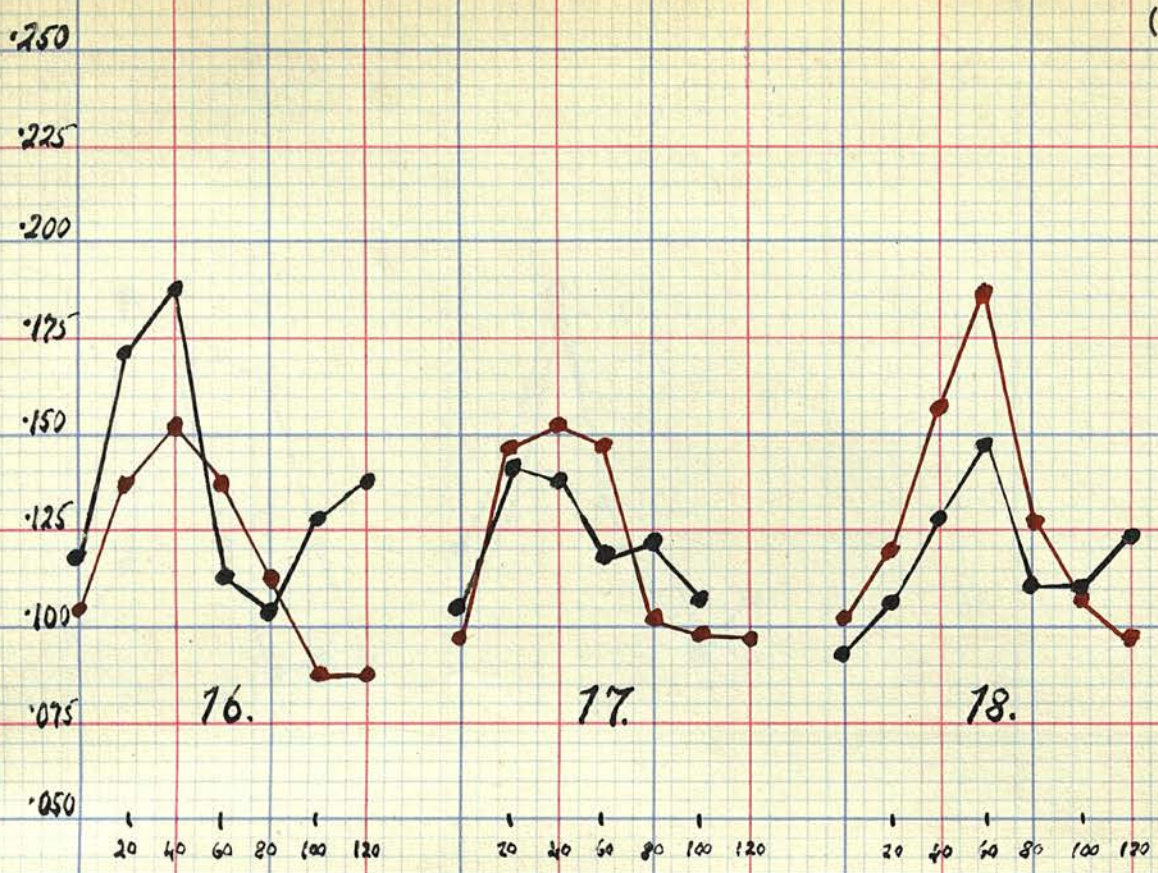
These results are expressed in the accompanying graphs. A number of the cases were repeated six months later and these readings are shown with the first readings. On the graphs the ordinary blood sugar curve is shown in red. This sugar curve is the one taken about the same time as the drug test was performed.

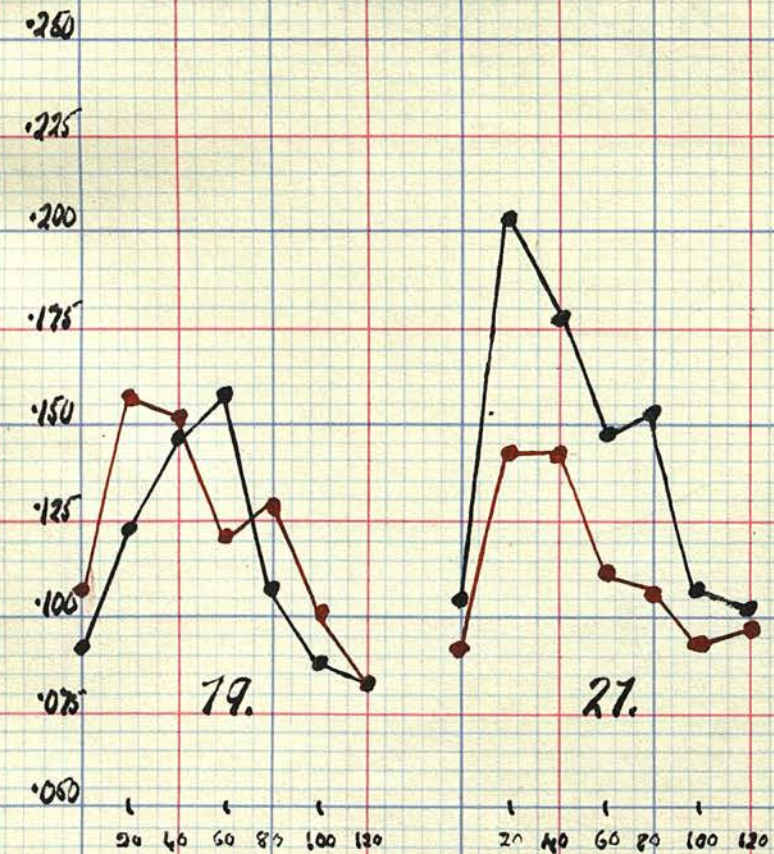
From the results it can be seen that the effect of atropine is to reduce the height of the blood sugar curve in Dementia Praecox. This action of atropine is also shown in the two normal curves though not to such a marked degree. In some of the cases of Dementia Praecox it is to be noted that the last figure approaches more to the fasting level than the ordinary ingestion curve.



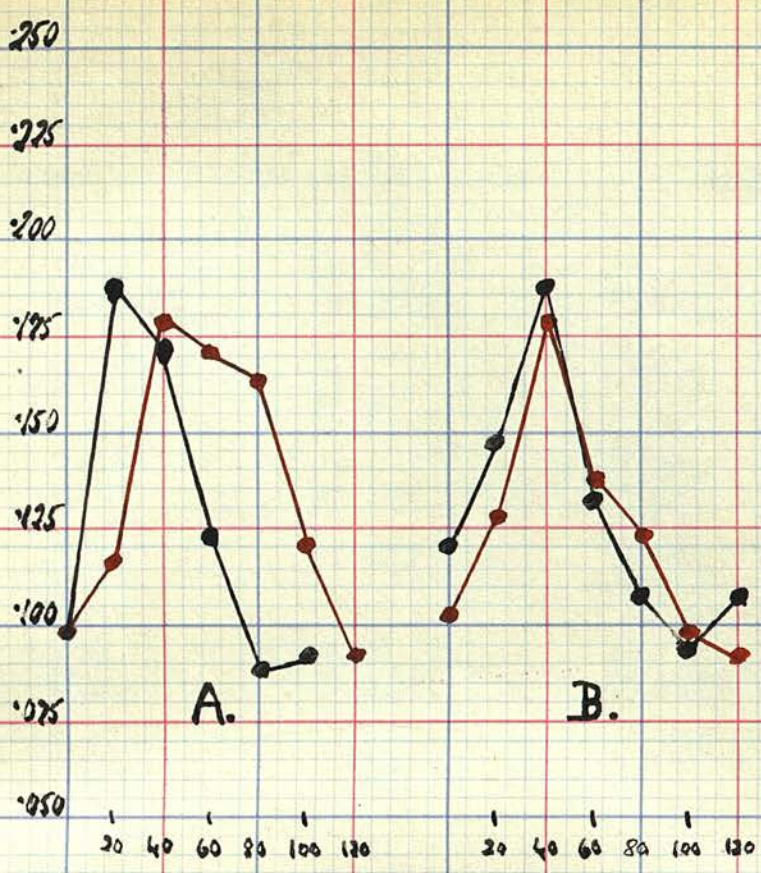


DEMENTIA PRAECOX Pilocarpine Nit. $\frac{1}{10}$ gr. 50 gm. Glucose.





DEMENTIA PRAECOX Pilocarpine Nit. $\frac{1}{10}$ gr. 50 gm. Glucose.



NORMAL Pilocarpine Nit. $\frac{1}{10}$ gr. 50 gm. Glucose.

Pilocarpine Nitrate $\frac{1}{10}$ gr. hypoderm.

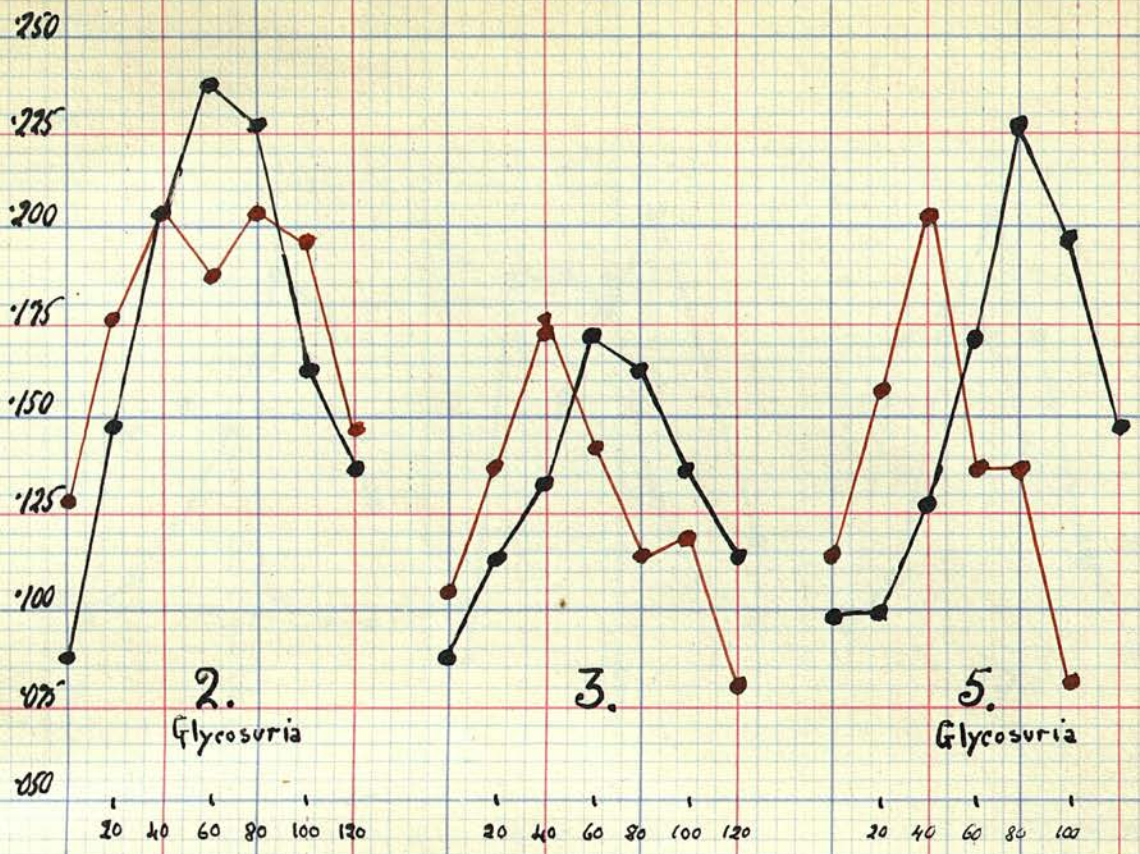
(2) 22.1.25	(3) 18.2.25	(5) 8.2.25	(6) 1.2.25
0.128	0.074	0.105	0.107
0.187	0.089	0.102	0.109
0.171	0.152	0.152	0.132
0.196	0.128	0.142	0.152
0.213	0.147	0.142	0.147
0.204	X	0.102	0.204
0.152	0.120	0.105	0.226

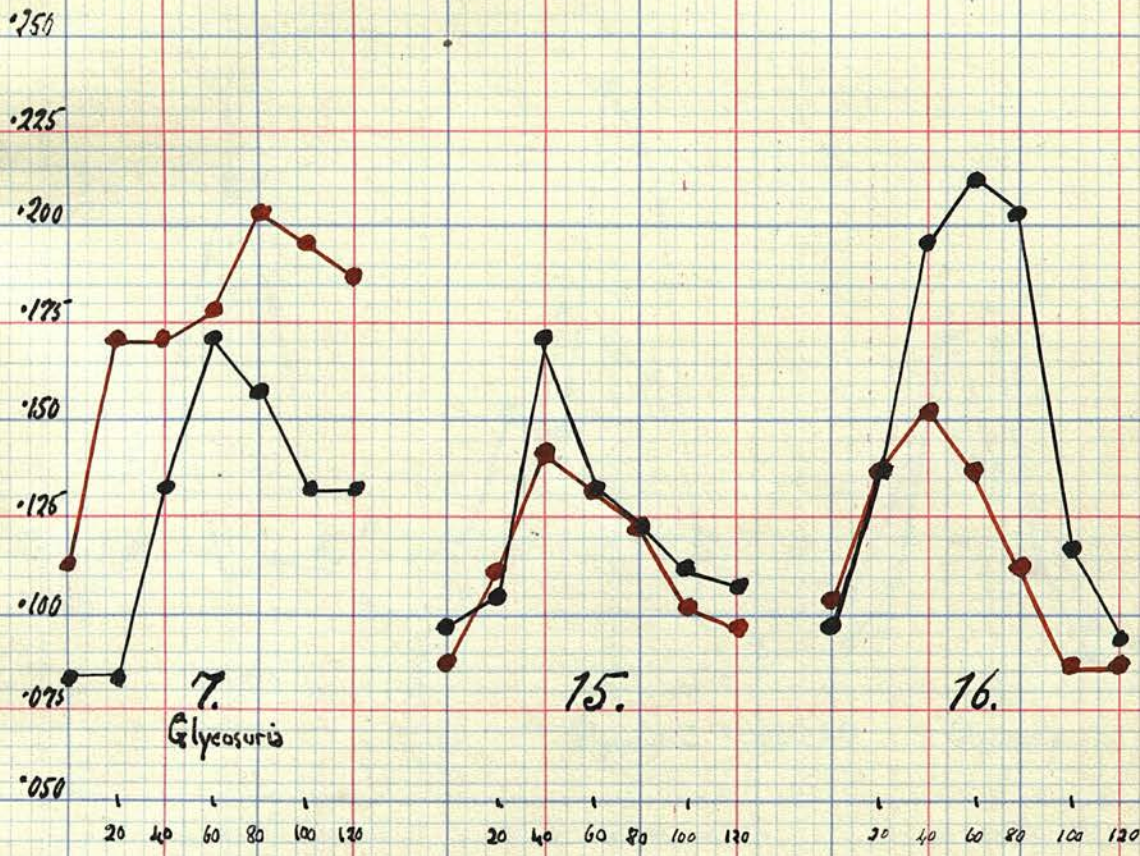
(7) 6.2.25	(15) 9.3.25	(16) 9.3.25	(17) 8.3.25
0.097	0.120	0.117	0.105
0.114	0.164	0.171	0.142
0.147	0.152	0.187	0.132
0.171	0.138	0.114	0.117
0.171	0.128	0.105	0.120
0.187	0.138	0.132	0.107
0.147	0.109	0.138	X

(18) 8.3.25	(19) 5.3.25	(21) 5.3.25
0.093	0.093	0.105
0.109	0.120	0.204
0.128	0.147	0.179
0.147	0.158	0.147
0.114	0.105	0.152
0.114	0.089	0.109
0.124	0.083	0.102

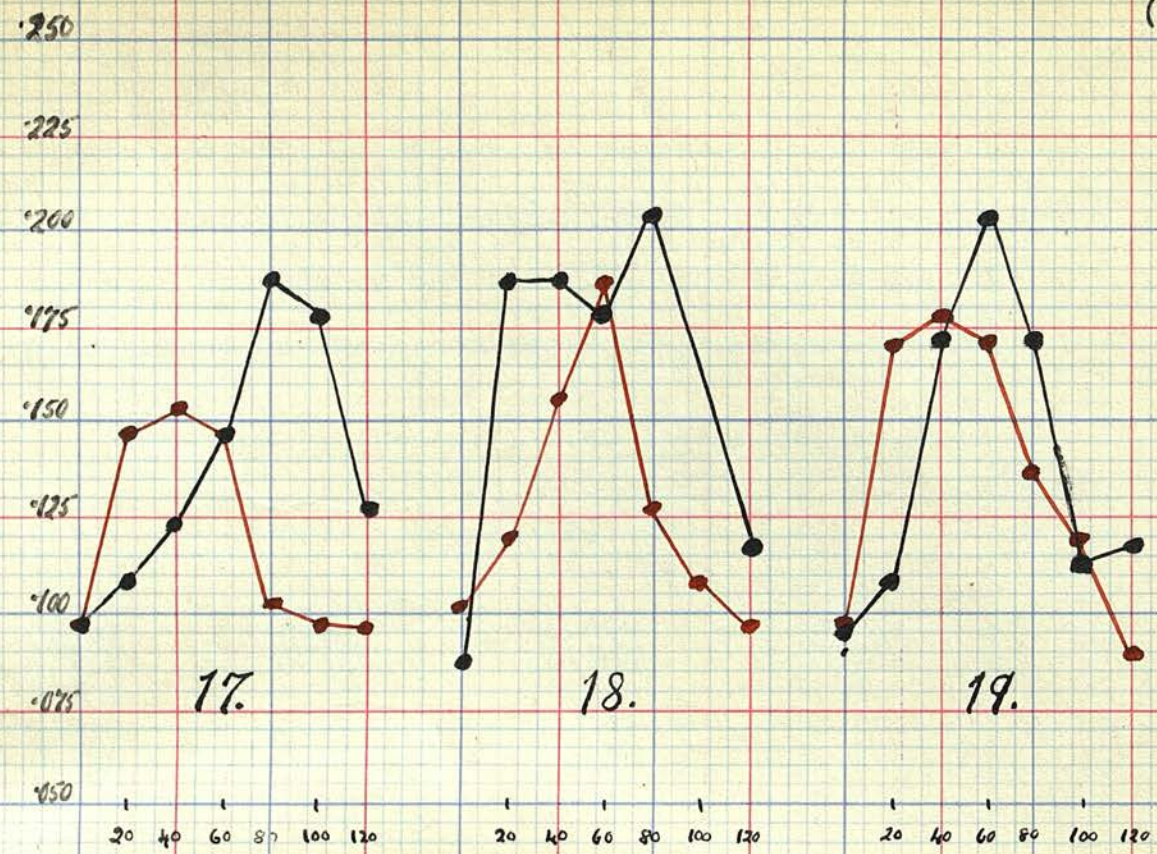
A.(Normal). 8.3.25	B.(Normal). 17.2.25
0.099	0.120
0.187	0.147
0.171	0.187
0.124	0.132
0.087	0.109
0.090	0.094
	0.107

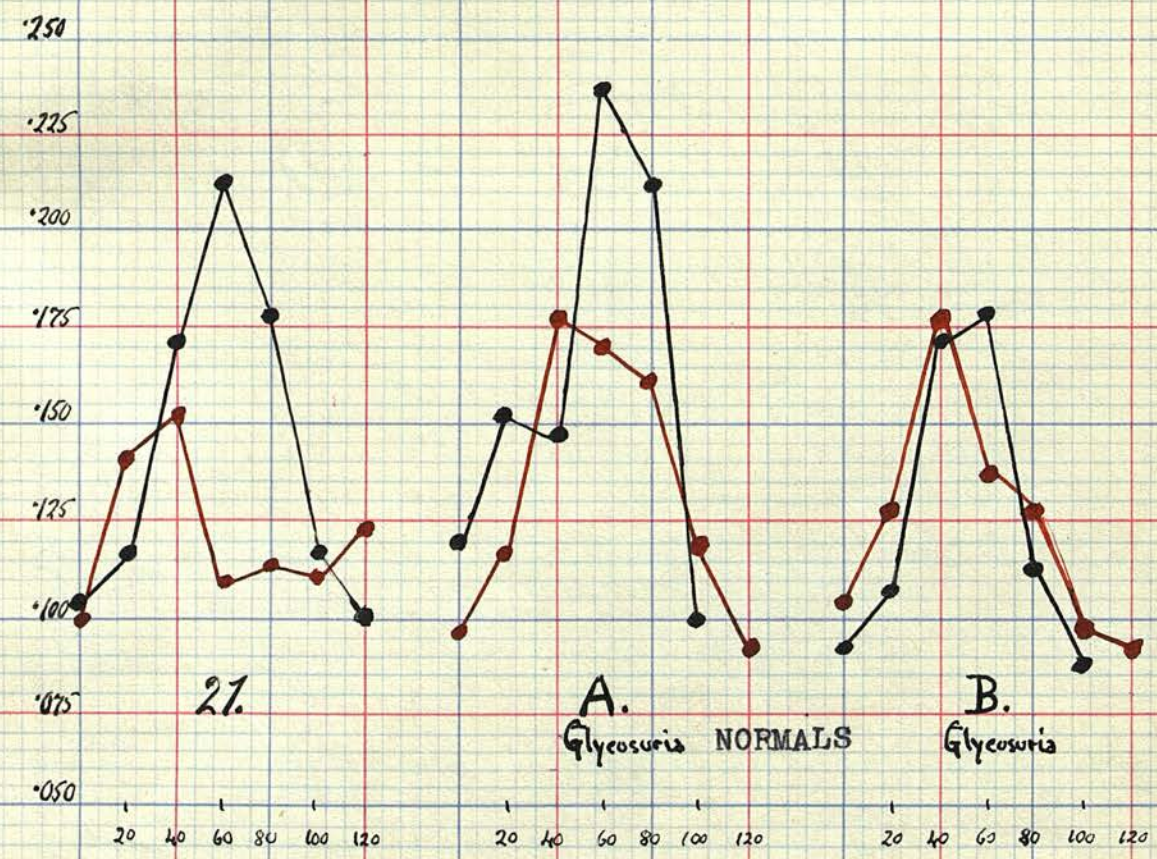
The results from pilocarpine injection do not give anything approaching uniformity, for while some





DEMENTIA Praecox. Pituitary (Infundin 1 c.c.) 50 gm. Glucose.





DEMENTIA PRAECOX. Pituitary (Infundin 1 c.c.) 50 gm.Glucose.

curves are raised, others are lowered. The two normals are slightly raised. From the results of these tests no conclusion can be drawn upon the action of pilocarpine on the blood sugar in Dementia Praecox.

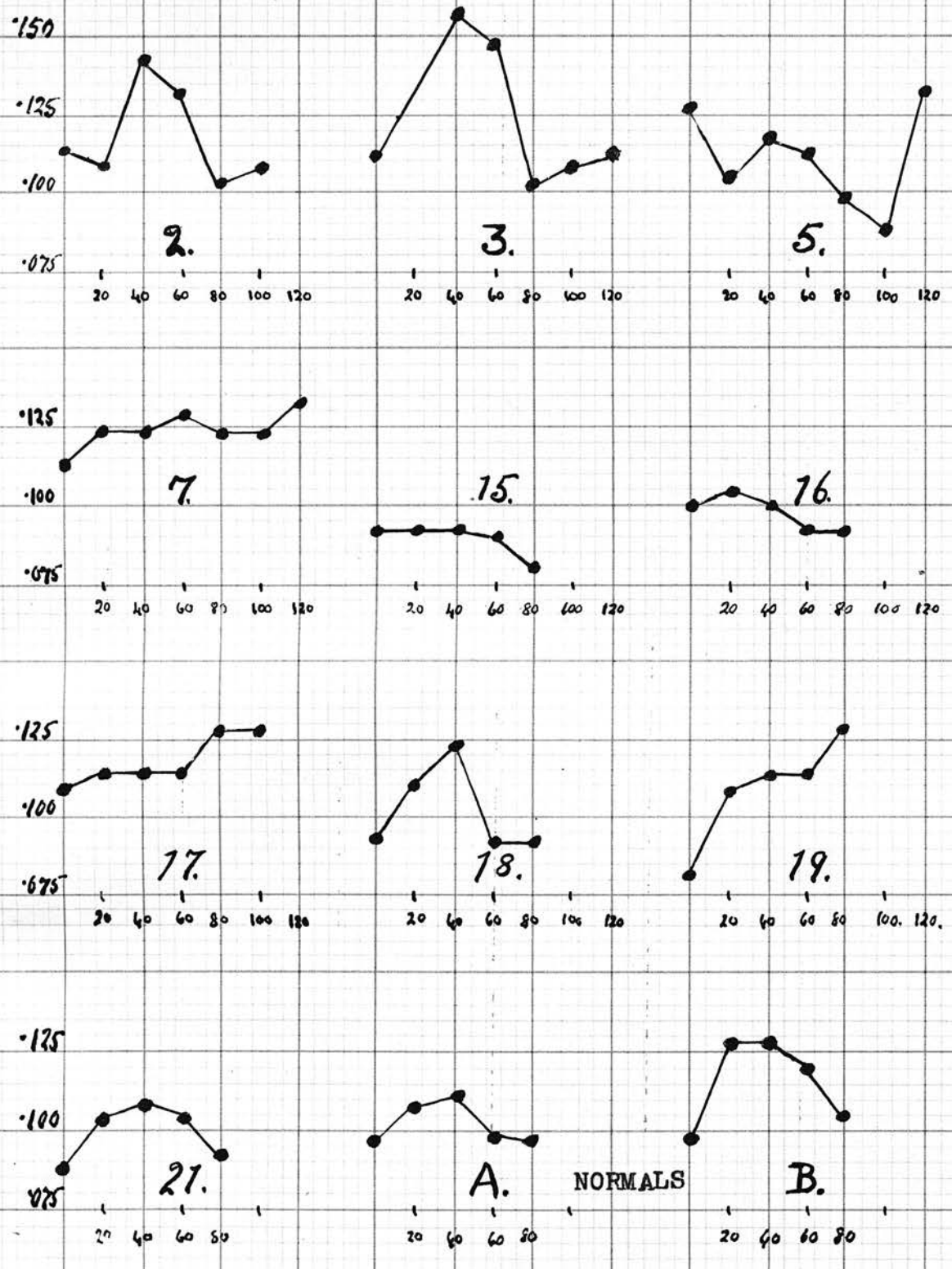
Pituitary (Infundin) 1 c.c. Intramuscularly.

(2) 28.1.25	(3) 4.2.25	(5) 15.2.25	(7) 13.2.25
0.087	0.089	0.099	0.084
0.147	0.114	0.100	0.084
0.204	0.132	0.128	0.132
0.238	0.171	0.171	0.171
0.226	0.164	0.226	0.158
0.164	0.138	0.196	0.132
0.138	0.114	0.147	0.132
Glyco-suria 1%.	Glyco-suria Nil.	Glyco-suria 4%	Glyco-suria 1%

(15) 18.3.25	(16) 18.3.25	(17) 15.3.25	(18) 15.3.25
0.099	0.097	0.097	0.087
0.105	0.138	0.109	0.187
0.171	0.196	0.124	0.187
0.132	0.213	0.147	0.179
0.124	0.204	0.187	0.204
0.111	0.117	0.179	X
0.109	0.094	0.128	0.117
Glyco-suria Nil.	Glyco-suria Nil.	Glyco-suria Nil	Glyco-suria Nil.

(19) 1.4.25	(21) 1.4.25	A.Normal. 20.2.25	B.Normal. 24.2.25
0.095	0.105	0.120	0.094
0.109	0.117	0.152	0.107
0.171	0.171	0.147	0.171
0.204	0.213	0.238	0.179
0.171	0.179	0.213	0.114
0.114	0.117	0.100	0.089
0.117	0.100	X	X
Glyco-suria Nil.	Glyco-suria Nil.	Glyco-suria 4%.	Glyco-suria 4%

The percentage of Glycosuria is from first



DEMENTIA PRAECOX Adrenalin 5 m. No Glucose.

quantity of urine passed after the test and not from a 24 hours collection.

These values show that the Dementia Praecox does not differ from the normal in the raising of the blood sugar as a result of pituitary injection. Case 7 is somewhat anomalous, the blood sugar curve is depressed and there is glycosuria which was not the case with the sugar meal alone, and this irregularity is also shown by Normal B. Case 3 shows no rise in the blood sugar as a result of pituitary injection, while 2, 5, 15, 17, 19 and 21 behave normally. Cases 16 and 18 show curves sustained above the accepted normal renal threshold (0.18 to 0.2) without glycosuria.

Adrenalin 5 m. hypoderm.(No glucose).

(2) 11.2.25	(3) 8.2.25	(5) 20.2.25	(7) 23.2.25
0.114	0.111	0.128	0.114
0.109	0.092	0.105	0.124
0.142	0.158	0.117	0.124
0.132	0.147	0.114	0.128
0.105	0.102	0.099	0.124
0.107	0.109	0.086	0.124
	0.111	0.132	0.132
(15) 27.3.25	(16) 27.3.25	(17) 22.3.25	(18) 22.3.25
0.093	0.100	0.109	0.094
0.094	0.105	0.114	0.111
0.093	0.100	0.114	0.124
0.090	0.093	0.114	0.094
0.081	0.093	0.128	0.093
		0.128	

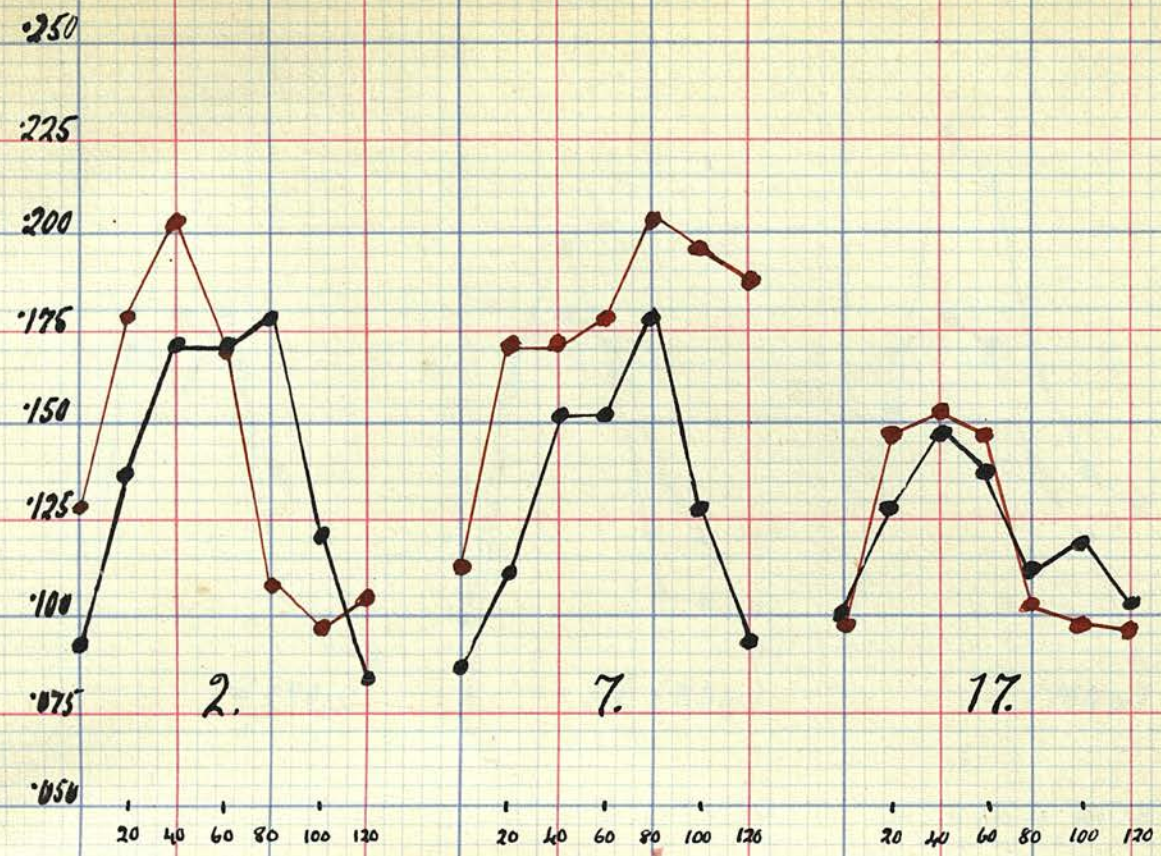
(19)	(21)	A.Normal.	B.Normal.
8.4.25	8.4.25	14.3.25	10.3.25
0.083	0.089	0.097	0.099
0.109	0.105	0.109	0.128
0.114	0.109	0.111	0.128
0.114	0.107	0.099	0.120
0.128	0.093	0.094	0.105

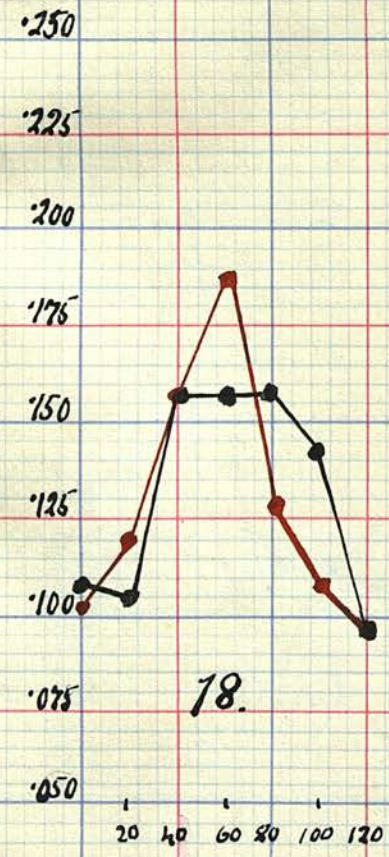
From these values it is seen that a short and temporary rise occurs in the blood sugar following the injection of adrenalin (V m.) in the normal. The rise is very small however and scarcely exceeds double the fallacy of the technique. This may be due to insufficient dosage but there is another objection in gauging the results of adrenalin injection, viz. absorption, the rate of which may give the result found. The values above are too varied and the reaction in the majority too small to form any conclusions.

Effect of Thyroid on the Blood Sugar Curve in Dementia Praecox.

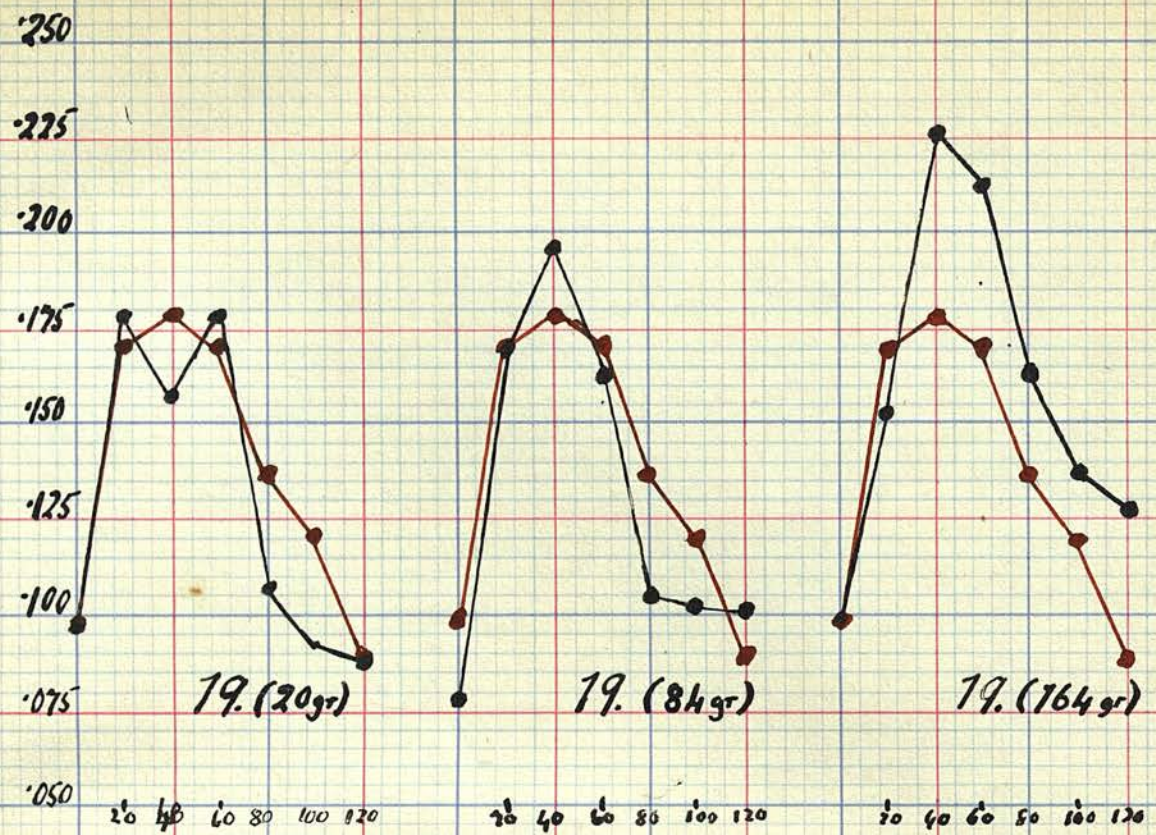
(19)

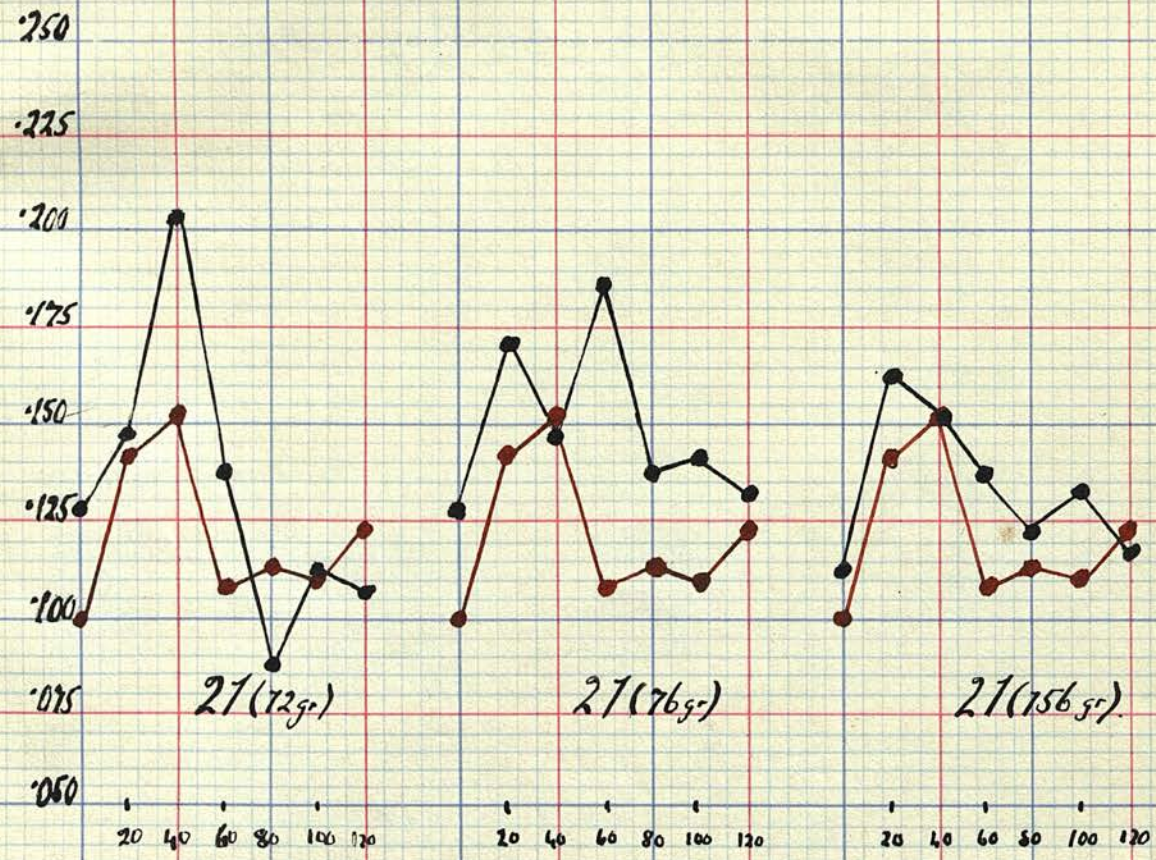
Before.	After. 2 grs.	20 grs.	84 grs.	164 grs = Total
2.2.25	5.2.25	9.2.25	12.2.25	19.2.25
0.099	0.102	0.097	0.079	0.099
0.171	0.164	0.179	0.171	0.152
0.179	0.204	0.158	0.196	0.226
0.171	0.179	0.179	0.164	0.213
0.138	0.079	0.107	0.105	0.164
0.120	0.087	0.093	0.102	0.138
0.090	0.099	0.087	0.100	0.128





DEMENTIA PRAECOX Thyroid Ext. (70 - 80 gr. over one week)





DEMENTIA PRAECOX Thyroid Ext. (Over two weeks).

(21)

Before.	After. 12 grs.	76 grs.	156 grs.
5.2.25	9.2.25	12.2.25	17.2.25
0.100	0.128	0.128	0.114
0.142	0.147	0.171	0.164
0.152	0.204	0.147	0.152
0.109	0.138	0.187	0.138
0.114	0.087	0.138	0.124
0.111	0.114	0.142	0.132
0.124	0.107	0.132	0.117

These two cases received more thyroid over a fortnight than the following which received about 70 to 80 grs. over a week.

(2)		(7)	
23.2.25	2.3.25	31.12.24	7.1.25
0.128	0.093	0.114	0.086
0.179	0.138	0.171	0.111
0.204	0.171	0.171	0.152
0.171	0.171	0.179	0.152
0.109	0.179	0.204	0.179
0.097	0.120	0.196	0.128
0.105	0.084	0.187	0.094

(17)		(18)	
22.2.25	5.4.25	22.2.25	5.4.25
0.097	0.100	0.102	0.109
0.147	0.128	0.120	0.105
0.152	0.147	0.158	0.158
0.147	0.138	0.187	0.158
0.102	0.111	0.128	0.158
0.099	0.120	0.109	0.142
0.097	0.102	0.097	0.097

From the results of thyroid feeding cases 19 and 21 show an increased blood sugar curve and in the case of the former a certain amount of delayed return.

This is what is usually associated with hyperthyroidism or ingestion of large amounts of thyroid (see page 27). The other cases do not show this. Case 7 shows but a slight rise while cases 2, 17 and 18 show a decrease in the height of the curve. Therefore four out of six cases do not respond to thyroid ingestion by hyperglycaemia. There was no glycosuria in these cases.

DISCUSSION.

Atropine depresses the blood sugar curve in Dementia Praecox and in the normal. The pharmacological action of atropine is to paralyse the myonneural junctions of the parasympathetic chiefly but not exclusively. The vagus stimulates the pancreas to secretion by direct stimulation (Pavlov) and through the action of secretion liberates by the gastric glands, whose activity is stimulated by the vagus. If the action of atropine by paralysing the vagal termination were to inhibit the internal secretion of the pancreas the result would be defective glycogenesis, but what is found is a low curve without evidence of this defect. But another action of atropine also brought about by its action on the parasympathetic is its arrest of secretions of the alimentary tract best demonstrated in the salivary glands. Such an action would

interfere with absorption and as previously noted, low blood sugar curves are to be regarded as chiefly due to defective absorption. This latter explanation would be the more feasible and simple one to account for the action of atropine on the blood sugar curves. Although this action is even both in normals and the Dementia Praecox, the effect is greater in the Dementia Praecox than in the normal, where the variation is slight. This difference may be due to a deficiency in the tone of the parasympathetic or more probably to the condition of the alimentary tract in Dementia Praecox, rendering absorption more difficult as these cases are like most psychoties, constipated.

The antagonism between atropine and pilocarpine would lead one to expect an opposite effect by the latter on the blood sugar. This is not borne out by these experiments on the Dementia Praecox, but the two normals show a slight increase, which, however, is not of sufficient degree to describe as a variation from the normal. Mann (5) employing a dose of $\frac{1}{20}$ gr. pilocarpine found no change in the blood sugar curve or depression followed by a rise. The results expressed here are anomalous, the depression of the sugar curve as in atropine is not so evident while the majority show no change or a raised curve. There is no evidence of an influence on the glycogenesis. If the vagal stimulus to the pancreas is to influence the glycogenesis, the action of pilo-

carpine

-carpine would be to accelerate the storage mechanism.

There is, however, the objection to these considerations, viz. that dosage must have an influence and the amount required to give a certain result may be the index of the effect.

These results do not give any information as to a possible influence of the vegetative nervous system and particularly the parasympathetic section on the carbohydrate metabolism, but only what is probably an absorption effect of atropine.

The remaining substances which were tried belong to the endocrine system.

Adrenaline acts as a stimulent to the sympathetic nerves myonneural junctions. Its action on the blood sugar is to accelerate the glycogenolysis in the liver by a similar action there. The normals responded by a small rise in the blood sugar while the cases of Dementia Praecox gave very varying results, some responding with a marked rise while others showed no response. The response to small injections of adrenalin would depend on rate of absorption (Shenk & Hermann Tronen), and as the glycogenolysis in response to adrenalin takes longer than its other actions there are too many fallacies to form any conclusion from these results.

The influence of pituitary on carbohydrate metabolism has been mentioned and the response on the part of the two normal controls give results in

accordance with it. The response in Dementia Praecox chiefly shows an increased curve but without glycosuria. This absence of glycosuria in most of the cases suggests a high renal threshold which is borne out by the numerous high sustained curves previously seen on ingestion of glucose also without glycosuria. Pituitary, however, has an action on the kidney causing diuresis probably due to a specific action on the renal cells. The occurence of glycosuria in three of the cases of Dementia Praecox which had previously high curves may be due to the hyperglycaemia induced by the pituitrin exceeding the already high renal threshold, or to a lowering of that threshold. The former view is the more feasible, as it is confirmed by the curves of two of the Dementia Praecox and the two normals. In which case such a curve as shown by 16 must have a very high threshold, as it is sustained at and above the 0.2 level for one hour.

The effect of thyroid feeding in Dementia Praecox shows that some cases respond by hyperglycaemia to a high level while the majority do not respond in this manner. Mann (5) describes the influence of thyroid therapy on cases of anxiety with depression and melamcholia with a delayed return curve approaching the normal with clinical improvement and the latter case with a normal type

curve giving as a result a high sustained curve and the clinical condition worse. Treatment was for one month.

The action of the thyroid and pituitary is to induce hyperglycaemia. From these results the pituitary appears to induce this result but the thyroid does not. In the cases examined all responded to the thyroid by tachycardia towards the end of the week to as much as 110 to 130 beats a minute, showing that absorption of the gland extract was producing clinical results.

That the blood sugar abnormalities are simply the expression of disordered carbohydrate metabolism in Dementia Praecox is fairly obvious and there is no evidence that it is directly connected with the mental state. Infective states, it has been noted, are frequently associated with a similar defect in sugar storage and an auto-infection has been put forward as being etiological in mental disorder. That auto-infection from the teeth or alimentary tract can aggravate a patient's mental condition is generally recognised. Relation between glycogenolysis and glycogenesis to the endocrines and vegetative nervous system is still most obscure. If the vegetative nervous system is the means of discharge of emotion (Cannon 16), then one would expect evidenceof dysfunction of that system in such a condition as Dementia Praecox, which displays marked

emotional abnormalities. That there is such dysfunction is supplied by clinical observation (v.s.) but for the abnormal blood sugar to be due to this the exact relation between the functions of the V.N.S. and the sugar metabolism must first be defined.
Vegetative Nervous System.

Concluding Summary.

From the results of these investigations the following conclusions are arrived at :-

(1) Dementia Praecox shows defective sugar storage in the majority of cases.

(2) Katatonia (Stupor) shows this defect more than Hebephrenia.

(3) That the renal threshold is raised in Dementia Praecox.

(4) That the injection of sympathomimetic and parasympathomimetic drugs do not afford evidence of any influence of the vegetative nervous system in the sugar curve.

(5) That the hyperglycaemia induced by ingestion of thyroid is not induced in four out of six cases of Dementia Praecox.

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